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(54) Title: GROUP B STREPTOCOCCUS ANTIGENS					
(57) Abstract					
Group B streptococcus (GBS) proteins and polynucleotides encoding them are disclosed. Said proteins are antigenic and therefore useful vaccine components for the prophylaxis or therapy of streptococcus infection in animals. Also disclosed are recombinant methods of producing the protein antigens as well as diagnostic assays for detecting streptococcus bacterial infection.					
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GROUP B STREPTOCOCCUS ANTIGENS

5

FIELD OF THE INVENTION

The present invention is related to antigens, more particularly protein antigens of group B streptococcus (GBS) bacterial pathogen which are useful as vaccine components for therapy and/or prophylaxis.

BACKGROUND OF THE INVENTION

15

Streptococcus are gram (+) bacteria that are differentiated by group specific carbohydrate antigens A through O found on their cell surface. Streptococcus groups are further distinguished by type-specific capsular polysaccharide antigens. Several serotypes have been identified for the Group B streptococcus (GBS) : Ia, Ib, II, III, IV, V, VI, VII and VIII. GBS also contains antigenic proteins known as "C-proteins" (alpha, beta, gamma and delta), some of which have been cloned.

25

Although GBS is a common component of the normal human vaginal and colonic flora this pathogen has long been recognized as a major cause of neonatal sepsis and meningitis, late-onset meningitis in infants, postpartum endometritis as well as mastitis in dairy herds. Expectant mothers exposed to GBS are at risk of postpartum infection and may transfer the infection to their baby as the child passes through the birth canal. Although the organism is sensitive to antibiotics, the high attack rate and rapid onset of sepsis in neonates and meningitis in infants results in high morbidity and mortality.

To find a vaccine that will protect individuals from GBS infection, researchers have turned to the type-specific antigens. Unfortunately these polysaccharides have proven to 5 be poorly immunogenic in humans and are restricted to the particular serotype from which the polysaccharide originates. Further, capsular polysaccharide elicit a T cell independent response i.e. no IgG production. Consequently capsular polysaccharide antigens are unsuitable 10 as a vaccine component for protection against GBS infection.

Others have focused on the C-protein beta antigen which demonstrated immunogenic properties in mice and rabbit models. This protein was found to be unsuitable as a human 15 vaccine because of its undesirable property of interacting with high affinity and in a non-immunogenic manner with the Fc region of human IgA. The C-protein alpha antigen is rare in type III serotypes of GBS which is the serotype responsible for most GBS mediated conditions and is 20 therefore of little use as a vaccine component.

Therefore there remains an unmet need for GBS antigens that may be used as vaccine components for the prophylaxis and/or 25 therapy of GBS infection.

SUMMARY OF THE INVENTION

30 According to one aspect, the present invention provides an isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide comprising a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
35 SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10,
SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15,
SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19,

SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
5 SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments,
analogous or derivatives thereof.

In other aspects, there is provided vectors comprising
polynucleotides of the invention operably linked to an
10 expression control region, as well as host cells transfected
with said vectors and methods of producing polypeptides
comprising culturing said host cells under conditions
suitable for expression.

15 In yet another aspect, there is provided novel polypeptides
encoded by polynucleotides of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

20 Figure 1a is the DNA sequence of clone 1 (SEQ ID NO :1) with
corresponding amino acid sequences for open reading frames;
figure 1b is the amino acid sequence SEQ ID NO: 2;
figure 1c is the amino acid sequence SEQ ID NO: 3;
25 figure 1d is the amino acid sequence SEQ ID NO: 4;
figure 1e is the amino acid sequence SEQ ID NO: 5;
figure 1f is the amino acid sequence SEQ ID NO: 6;

Figure 2a is the DNA sequence of clone 2 (SEQ ID NO :7) with
30 corresponding amino acid sequences for open reading frames;
figure 2b is the amino acid sequence SEQ ID NO: 8;
figure 2c is the amino acid sequence SEQ ID NO: 9;
figure 2d is the amino acid sequence SEQ ID NO:10;
figure 2e is the amino acid sequence SEQ ID NO:11;
35 figure 2f is the amino acid sequence SEQ ID NO:12;

Figure 3a is the DNA sequence of clone 3 (SEQ ID NO :13) with corresponding amino acid sequences for open reading frames;

5 figure 3b is the amino acid sequence SEQ ID NO:14;

figure 3c is the amino acid sequence SEQ ID NO:15;

figure 3d is the amino acid sequence SEQ ID NO:16;

figure 3e is the amino acid sequence SEQ ID NO:17;

figure 3f is the amino acid sequence SEQ ID NO:18;

figure 3g is the amino acid sequence SEQ ID NO:19;

10 figure 3h is the amino acid sequence SEQ ID NO:20;

figure 3i is the amino acid sequence SEQ ID NO:21;

Figure 4a is the DNA sequence of clone 4 (SEQ ID NO :22)

with corresponding amino acid sequences for open reading

15 frames;

figure 4b is the amino acid sequence SEQ ID NO:23;

figure 4c is the amino acid sequence SEQ ID NO:24;

figure 4d is the amino acid sequence SEQ ID NO:25;

figure 4e is the amino acid sequence SEQ ID NO:26;

20

Figure 5a is the DNA sequence of clone 5 (SEQ ID NO :27)

with corresponding amino acid sequences for open reading

frames;

figure 5b is the amino acid sequence SEQ ID NO:28;

25 figure 5c is the amino acid sequence SEQ ID NO:29;

figure 5d is the amino acid sequence SEQ ID NO:30;

figure 5e is the amino acid sequence SEQ ID NO:31;

Figure 6a is the DNA sequence of clone 6 (SEQ ID NO :32) ;

30 figure 6b is the amino acid sequence SEQ ID NO:33;

figure 6c is the amino acid sequence SEQ ID NO:34;

figure 6d is the amino acid sequence SEQ ID NO:35;

figure 6e is the amino acid sequence SEQ ID NO:36;

35 Figure 7a is the DNA sequence of clone 7 (SEQ ID NO :37) ;

figure 7b is the amino acid sequence SEQ ID NO:38;

figure 7c is the amino acid sequence SEQ ID NO:39;
figure 7d is the amino acid sequence SEQ ID NO:40;
figure 7e is the amino acid sequence SEQ ID NO:41;

5 Figure 8 is the DNA sequence of a part of clone 7 including
a signal sequence (SEQ ID NO :42);

Figure 9 is the DNA sequence of a part of clone 7 without a
signal sequence (SEQ ID NO :43);

10 Figure 9a is the amino acid sequence (SEQ ID NO:44);

Figure 10 represents the distribution of anti-GBS ELISA
titers in sera from CD-1 mice immunized with recombinant GBS
protein corresponding to the SEQ ID NO:39.

DETAILED DESCRIPTION OF THE INVENTION

The present invention relates to novel antigenic polypeptides of group B streptococcus (GBS) characterized by

5 the amino acid sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10,

SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15,

10 SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19,
SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24,

SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 29,

SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34,

SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 39,

15 SEQ ID NO: 40, SEQ ID NO: 41 and SEQ ID NO: 44 or fragments,
analogous or derivatives thereof.

A preferred embodiment of the invention includes SEQ ID NO :39 and SEQ ID NO:44.

20 A further preferred embodiment of the invention is SEQ ID NO :39.

25 A further preferred embodiment of the invention is SEQ ID NO :44.

As used herein, "fragments", "derivatives" or "analogous" of the polypeptides of the invention include those polypeptides in which one or more of the amino acid residues are

30 substituted with a conserved or non-conserved amino acid residue (preferably conserved) and which may be natural or unnatural.

35 The terms «fragments», «derivatives» or «analogues» of polypeptides of the present invention also include polypeptides which are modified by addition, deletion,

substitution of amino acids provided that the polypeptides retain the capacity to induce an immune response.

By the term «conserved amino acid» is meant a substitution 5 of one or more amino acids for another in which the antigenic determinant (including its secondary structure and hydropathic nature) of a given antigen is completely or partially conserved in spite of the substitution.

10 For example, one or more amino acid residues within the sequence can be substituted by another amino acid of a similar polarity, which acts as a functional equivalent, resulting in a silent alteration. Substitutes for an amino acid within the sequence may be selected from other members 15 of the class to which the amino acid belongs. For example, the nonpolar (hydrophobic) amino acids include alanine, leucine, isoleucine, valine, proline, phenylalanine, tryptophan and methionine. The polar neutral amino acids include glycine, serine, threonine, cysteine, tyrosine, 20 asparagine and glutamine. The positively charged (basic) amino acids include arginine, lysine and histidine. The negatively charged (acidic) amino acids include aspartic acid and glutamic acid.

25 Preferably, derivatives and analogs of polypeptides of the invention will have about 70% identity with those sequences illustrated in the figures or fragments thereof. That is, 70% of the residues are the same. More preferably polypeptides will have greater than 95% homology. In another 30 preferred embodiment, derivatives and analogs of polypeptides of the invention will have fewer than about 20 amino acid residue substitutions, modifications or deletions and more preferably less than 10. Preferred substitutions are those known in the art as conserved i.e. the substituted 35 residues share physical or chemical properties such as hydrophobicity, size, charge or functional groups.

Furthermore, in those situations where amino acid regions are found to be polymorphic, it may be desirable to vary one or more particular amino acids to more effectively mimic the 5 different epitopes of the different GBS strains.

Also included are polypeptides which have fused thereto other compounds which alter the polypeptides biological or pharmacological properties i.e. polyethylene glycol (PEG) to 10 increase half-life; leader or secretory amino acid sequences for ease of purification; prepro- and pro- sequences; and (poly)saccharides.

Moreover, the polypeptides of the present invention can be 15 modified by terminal -NH₂ acylation (eg. by acetylation, or thioglycolic acid amidation, terminal carbosy amidation, e.g. with ammonia or methylamine) to provide stability, increased hydrophobicity for linking or binding to a support or other molecule.

20 Also contemplated are hetero and homo polypeptide multimers of the polypeptide fragments, analogues and derivatives. These polymeric forms include, for example, one or more polypeptides that have been cross-linked with cross-linkers 25 such as avidin/biotin, gluteraldehyde or dimethyl-superimide. Such polymeric forms also include polypeptides containing two or more tandem or inverted contiguous sequences, produced from multicistronic mRNAs generated by recombinant DNA technology.

30 Preferably, a fragment, analog or derivative of a polypeptide of the invention will comprise at least one antigenic region i.e. at least one epitope.

35 In order to achieve the formation of antigenic polymers (i.e. synthetic multimers), polypeptides may be utilized having bishaloacetyl groups, nitroarylhalides, or the like,

where the reagents being specific for thio groups. Therefore, the link between two mercapto groups of the different peptides may be a single bond or may be composed of a linking group of at least two, typically at least four, 5 and not more than 16, but usually not more than about 14 carbon atoms.

In a particular embodiment, polypeptide fragments, analogs and derivatives of the invention do not contain a methionine 10 (Met) starting residue. Preferably, polypeptides will not incorporate a leader or secretory sequence (signal sequence). The signal portion of a polypeptide of the invention may be determined according to established molecular biological techniques. In general, the 15 polypeptide of interest may be isolated from a GBS culture and subsequently sequenced to determine the initial residue of the mature protein and therefor the sequence of the mature polypeptide.

20 According to another aspect, there is provided vaccine compositions comprising one or more GBS polypeptides of the invention in admixture with a pharmaceutically acceptable carrier diluent or adjuvant.

25 Suitable adjuvants include oils i.e. Freund's complete or incomplete adjuvant; salts i.e. $AlK(SO_4)_2$, $AlNa(SO_4)_2$, $AlNH_4(SO_4)_2$, $Al(OH)_3$, $AlPO_4$, silica, kaolin; saponin derivative; carbon polynucleotides i.e. poly IC and poly AU and also detoxified cholera toxin (CTB) and E.coli heat 30 labile toxin for induction of mucosal immunity. Preferred adjuvants include QuilATM, AlhydrogelTM and AdjuphosTM. Vaccines of the invention may be administered parenterally by injection, rapid infusion, nasopharyngeal absorption, dermoabsorption, or bucal or oral.

Vaccine compositions of the invention are used for the treatment or prophylaxis of *streptococcus* infection and/or diseases and symptoms mediated by *streptococcus* infection, 5 in particular group A *streptococcus* (*pyogenes*), group B *streptococcus* (GBS or *agalactiae*), *dysgalactiae*, *uberis*, *nocardia* as well as *Staphylococcus aureus*. General information about *Streptococcus* is available in Manual of Clinical Microbiology by P.R.Murray et al. (1995, 6th Edition, 10 ASM Press, Washington, D.C.). More particularly group B *streptococcus*, *agalactiae*. In a particular embodiment vaccines are administered to those individuals at risk of GBS infection such as pregnant women and infants for sepsis, meningitis and pneumonia as well as immunocompromised 15 individuals such as those with diabetes, liver disease or cancer. Vaccines may also have veterinary applications such as for the treatment of mastitis in cattle which is mediated by the above mentioned bacteria as well as *E.coli*.

20 The vaccine of the present invention can also be used for the manufacture of a medicament used for the treatment or prophylaxis of *streptococcus* infection and/or diseases and symptoms mediated by *streptococcus* infection, in particular group A *streptococcus* (*pyogenes*), group B *streptococcus* (GBS 25 or *agalactiae*), *dysgalactiae*, *uberis*, *nocardia* as well as *Staphylococcus aureus*. More particularly group B *streptococcus*, *agalactiae*.

Vaccine compositions are preferably in unit dosage form of 30 about 0.001 to 100 µg/kg (antigen/body weight) and more preferably 0.01 to 10 µg/kg and most preferably 0.1 to 1 µg/kg 1 to 3 times with an interval of about 1 to 12 weeks intervals between immunizations, and more preferably 1 to 6

weeks.

According to another aspect, there is provided polynucleotides encoding polypeptides of group B
5 streptococcus (GBS) characterized by the amino acid sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,

10 SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,

SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,

15 SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments,
analogous or derivatives thereof.

Preferred polynucleotides are those illustrated in figures 1a (SEQ ID NO: 1), 2a (SEQ ID NO: 7), 3a (SEQ ID NO: 13), 4a
20 (SEQ ID NO: 22), 5a (SEQ ID NO: 27), 6a (SEQ ID NO: 32), 7a
(SEQ ID NO: 37), 8 (SEQ ID NO : 42) and 9(SEQ ID NO : 43)
which correspond to the open reading frames, encoding
polypeptides of the invention.

25 Preferred polynucleotides are those illustrated in figures 1a (SEQ ID NO: 1), 2a (SEQ ID NO: 7), 3a (SEQ ID NO: 13), 4a
(SEQ ID NO: 22), 5a (SEQ ID NO: 27), 6a (SEQ ID NO: 32), 7a
(SEQ ID NO: 37), 8 (SEQ ID NO : 42) and 9(SEQ ID NO : 43)
and fragments, analogues and derivatives thereof.

30 More preferred polynucleotides of the invention are those illustrated in Figures 7 (SEQ ID NO : 37), 8 (SEQ ID NO : 42) and 9(SEQ ID NO : 43).

35 Most preferred polynucleotides of the invention are those illustrated in Figures 8 (SEQ ID NO : 42) and 9(SEQ ID NO :

43).

It will be appreciated that the polynucleotide sequences illustrated in the figures may be altered with degenerate 5 codons yet still encode the polypeptides of the invention.

Due to the degeneracy of nucleotide coding sequences, other polynucleotide sequences which encode for substantially the same polypeptides of the present invention may be used in 10 the practice of the present invention. These include but are not limited to nucleotide sequences which are altered by the substitution of different codons that encode the same amino acid residue within the sequence, thus producing a silent change.

15

Accordingly the present invention further provides polynucleotides which hybridize to the polynucleotide sequences herein above described (or the complement sequences thereof) having 50% and preferably at least 70% 20 identity between sequences. More preferably polynucleotides are hybridizable under stringent conditions i.e. having at least 95% identity and most preferably more than 97% identity.

25 By capable of hybridizing under stringent conditions is meant annealing of a nucleic acid molecule to at least a region of a second nucleic acid sequence (whether as cDNA, mRNA, or genomic DNA) or to its complementary strand under standard conditions, e.g. high temperature and/or low salt 30 content, which tend to disfavor hybridization of noncomplementary nucleotide sequences. A suitable protocol is described in Maniatis T. et al., Molecular cloning : A Laboratory Manual, Cold Springs Harbor Laboratory, 1982, which is herein incorporated by reference.

35

In a further aspect, polynucleotides encoding polypeptides

of the invention, or fragments, analogs or derivatives thereof, may be used in a DNA immunization method. That is, they can be incorporated into a vector which is replicable and expressible upon injection thereby producing
5 the antigenic polypeptide in vivo. For example polynucleotides may be incorporated into a plasmid vector under the control of the CMV promoter which is functional in eukaryotic cells. Preferably the vector is injected intramuscularly.

10

According to another aspect, there is provided a process for producing polypeptides of the invention by recombinant techniques by expressing a polynucleotide encoding said polypeptide in a host cell and recovering the expressed
15 polypeptide product. Alternatively, the polypeptides can be produced according to established synthetic chemical techniques i.e. solution phase or solid phase synthesis of oligopeptides which are ligated to produce the full polypeptide (block ligation).

20

For recombinant production, host cells are transfected with vectors which encode the polypeptide, and then cultured in a nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes.
25 Suitable vectors are those that are viable and replicable in the chosen host and include chromosomal, non-chromosomal and synthetic DNA sequences e.g. bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA. The polypeptide
30 sequence may be incorporated in the vector at the appropriate site using restriction enzymes such that it is operably linked to an expression control region comprising a promoter, ribosome binding site (consensus region or Shine-Dalgarno sequence), and optionally an operator (control
35 element). One can select individual components of the expression control region that are appropriate for a given

host and vector according to established molecular biology principles (Sambrook et al, Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor, N.Y., 1989 incorporated herein by reference). Suitable promoters include but are not limited to LTR or SV40 promoter, *E.coli* lac, tac or trp promoters and the phage lambda P_L promoter. Vectors will preferably incorporate an origin of replication as well as selection markers i.e. ampicillin resistance gene. Suitable bacterial vectors include pET, pQE70, pQE60, pQE-9, pbs, pD10 phagescript, psiX174, pbluescript SK, pbsks, pNH8A, pNH16a, pNH18A, pNH46A, ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 and eukaryotic vectors pBlueBacIII, pWLNEO, pSV2CAT, pOG44, pXT1, pSG, pSVK3, pBPV, pMSG and pSVL. Host cells may be bacterial i.e. *E.coli*, *Bacillus subtilis*, *Streptomyces*; fungal i.e. *Aspergillus niger*, *Aspergillus nidulans*; yeast i.e. *Saccharomyces* or eukaryotic i.e. CHO, COS.

Upon expression of the polypeptide in culture, cells are typically harvested by centrifugation then disrupted by physical or chemical means (if the expressed polypeptide is not secreted into the media) and the resulting crude extract retained to isolate the polypeptide of interest. Purification of the polypeptide from culture media or lysate may be achieved by established techniques depending on the properties of the polypeptide i.e. using ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, hydroxylapatite chromatography and lectin chromatography. Final purification may be achieved using HPLC.

The polypeptide may be expressed with or without a leader or secretion sequence. In the former case the leader may be removed using post-translational processing (see US

4,431,739; 4,425,437; and 4,338,397 incorporated herein by reference) or be chemically removed subsequent to purifying the expressed polypeptide.

5 According to a further aspect, the GBS polypeptides of the invention may be used in a diagnostic test for streptococcus infection in particular GBS infection. Several diagnostic methods are possible, for example detecting streptococcus organism in a biological sample, the following procedure may
10 be followed:

- a) obtaining a biological sample from a patient;
- b) incubating an antibody or fragment thereof reactive with a GBS polypeptide of the invention with the biological sample to form a mixture; and
- 15 c) detecting specifically bound antibody or bound fragment in the mixture which indicates the presence of streptococcus.

20 Alternatively, a method for the detection of antibody specific to a streptococcus antigen in a biological sample containing or suspected of containing said antibody may be performed as follows:

- a) isolating a biological sample from a patient;
- b) incubating one or more GBS polypeptides of the
25 invention or fragments thereof with the biological sample to form a mixture; and
- c) detecting specifically bound antigen or bound fragment in the mixture which indicates the presence of antibody specific to streptococcus.

30 One of skill in the art will recognize that this diagnostic test may take several forms, including an immunological test such as an enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay or a latex agglutination assay, essentially
35 to determine whether antibodies specific for the protein are present in an organism.

The DNA sequences encoding polypeptides of the invention may also be used to design DNA probes for use in detecting the presence of streptococcus in a biological sample suspected 5 of containing such bacteria. The detection method of this invention comprises:

- a) isolating the biological sample from a patient;
- b) incubating one or more DNA probes having a DNA sequence 10 encoding a polypeptide of the invention or fragments thereof with the biological sample to form a mixture; and
- c) detecting specifically bound DNA probe in the mixture which indicates the presence of streptococcus bacteria.

15 The DNA probes of this invention may also be used for detecting circulating streptococcus i.e. GBS nucleic acids in a sample, for example using a polymerase chain reaction, as a method of diagnosing streptococcus infections. The probe may be synthesized using conventional techniques and 20 may be immobilized on a solid phase, or may be labeled with a detectable label. A preferred DNA probe for this application is an oligomer having a sequence complementary to at least about 6 contiguous nucleotides of the GBS polypeptides of the invention.

25 Another diagnostic method for the detection of streptococcus in a patient comprises:

- a) labeling an antibody reactive with a polypeptide of the invention or fragment thereof with a detectable label;
- 30 b) administering the labeled antibody or labeled fragment to the patient; and
- c) detecting specifically bound labeled antibody or labeled fragment in the patient which indicates the presence of streptococcus.

35 A further aspect of the invention is the use of the GBS

polypeptides of the invention as immunogens for the production of specific antibodies for the diagnosis and in particular the treatment of streptococcus infection.

Suitable antibodies may be determined using appropriate

5 screening methods, for example by measuring the ability of a particular antibody to passively protect against streptococcus infection in a test model. One example of an animal model is the mouse model described in the examples herein. The antibody may be a whole antibody or an antigen-
10 binding fragment thereof and may in general belong to any immunoglobulin class. The antibody or fragment may be of animal origin, specifically of mammalian origin and more specifically of murine, rat or human origin. It may be a natural antibody or a fragment thereof, or if desired, a
15 recombinant antibody or antibody fragment. The term recombinant antibody or antibody fragment means antibody or antibody fragment which were produced using molecular biology techniques. The antibody or antibody fragments may be polyclonal, or preferably monoclonal. It may be specific
20 for a number of epitopes associated with the GBS polypeptides but is preferably specific for one.

EXAMPLE 1 Murine model of lethal Group B Streptococcus (GBS)
25 infection

The mouse model of GBS infection is described in detail in Lancefield et al (J Exp Med 142:165-179, 1975). GBS strain C388/90 (Clinical isolate obtained in 1990 from the

30 cephalorachidian fluid of a patient suffering from meningitis, Children's Hospital of Eastern Ontario, Ottawa, Canada) and NCS246 (National Center for Streptococcus, Provincial Laboratory of Public Health for Northern Alberta, Edmonton, Canada) were respectively serotyped as type Ia/c
35 and type II/R.

To increase their virulence, the GBS strains C388/90 (serotype Ia/c) and NCS 246 (serotype II/R) were serially passaged through mice as described previously (Lancefield et al. J Exp Med 142:165-179, 1975). Briefly, the increase of 5 virulence was monitored using intraperitoneal inoculations of serial dilutions of a subculture in Todd-Hewitt broth obtained from either the blood or spleen of infected mice. After the last passage, infected blood samples were used to inoculate Todd-Hewitt broth. After an incubation of 2 hours 10 at 37°C with 7% CO₂, glycerol at a final concentration of 10% (v/v) was added to the culture. The culture was then aliquoted and stored at -80° C for use in GBS challenge experiments. The number of cfu of GBS present in these frozen samples was determined. The bacterial concentration 15 necessary to kill 100% (LD100) of the 18 weeks old mice were determined to be 3.5X10⁵ and 1.1X10⁵ respectively for GBS strain C388/90 and NCS246, which corresponded to a significant increase in virulence for both strains. Indeed, the LD100 recorded before the passages for these two strains 20 was higher than 10⁹ cfu.

In a bacterial challenge, a freshly thawed aliquot of a virulent GBS strain was adjusted to the appropriate bacterial concentration using Todd-Hewitt broth and 1ml was 25 injected intraperitoneally to each female CD-1 mouse. The mice used for the passive protection experiments were 6 to 8 weeks old, while the ones used for the active protection experiments were approximately 18 weeks old at the time of the challenge. All inocula were verified by colony counts. 30 Animals were observed for any sign of infection four times daily for the first 48 h after challenge and then daily for the next 12 days. At the end of that period, blood samples were obtained from the survivors and frozen at -20°C. The spleen obtained from each mouse that survived the challenge 35 was cultured in order to identify any remaining GBS.

EXAMPLE 2 Immunization and protection in mice with formaldehyde killed whole GBS cells

5 Formaldehyde killed GBS whole cells were prepared according to the procedures described in Lancefield et al (J Exp Med 142:165-179, 1975). Briefly, an overnight culture on sheep blood agar plates (Quelab Laboratories, Montreal, Canada) of a GBS strain was washed twice in PBS buffer (phosphate buffered-saline, pH7.2), adjusted to approximately 3×10^9 cfu/mL and incubated overnight in PBS containing 0.3% (v/v) formaldehyde. The killed GBS suspension was washed with PBS and kept frozen at -80°C.

10

15 Female CD-1 mice, 6 to 8 weeks old (Charles River, St-Constant, Québec, Canada), were injected subcutaneously three times at two weeks interval with 0.1 ml of formaldehyde killed cells of GBS strain C388/90 ($\sim 6 \times 10^7$ GBS), or 0.1 ml of PBS for the control group. On the day before

20 the immunization, Alhydrogel™ (Superfos Biosector, Frederikssund, Denmark) at a final concentration of 0.14 mg or 0.21 mg of Al, was added to these preparations and incubated overnight at 4°C with agitation. Serum samples were obtained from each mouse before the beginning of the

25 immunization protocol and two weeks after the last injection. The sera were frozen at -20°C.

30 Eight mice in each control group injected with PBS and the group immunized with formaldehyde killed whole cells GBS strain C388/90 (Ia/c) were challenged with 1.5×10^4 cfu of GBS strain C388/90 (Ia/c) one week after the third injection. All mice immunized with the formaldehyde killed GBS whole cells survived the homologous challenge while, within 5 days after the challenge, only 4 out of the 8 mice

35 injected with PBS survived from the infection. In order to increase the mortality rate in the control groups, the

bacterial suspension had to be adjusted according to the age of the mice at the time of the bacterial challenge. In subsequent challenge experiments, when mice were older than 15 weeks, the bacterial inoculum was increased to 5 concentrations between 3.0×10^5 and 2.5×10^6 cfu.

Table 1 Immunization of CD1 mice with formaldehyde killed whole cells of GBS and subsequent homologous challenge [strain C388/90 (Ia/c)] and heterologous challenge [strain NCS246 (II/R)].

antigenic preparations used for immunization ¹	number of living mice 14 days after the bacterial challenge (% Survival)	
	homologous challenge: strain C388/90 (Ia/c)	heterologous challenge: strain NCS246 (II/R)
1st infection		
formaldehyde killed cells of GBS strain C388/90 (Ia/c) ²	8/8 (100) ³	n.d. ⁵
control PBS	4/8 (50)	n.d.
2nd infection		
formaldehyde killed cells of GBS strain C388/90 (Ia/c)	6/6 (100) ⁴	0/6 (0) ⁶
control PBS	2/6 (33)	0/6 (0)

¹ alhydrogel™ at a final concentration of 0.14 mg or 0.21mg of Al was used;

² approximately 6×10^7 cfu;

³ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 1.5×10^4 cfu;

⁴ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 2.1×10^6 cfu;

⁵ not done;

⁶ intraperitoneal challenge with 1 mL Todd-Hewitt culture medium containing GBS NCS246 (II/R) suspension adjusted to 1.2×10^5 cfu.

In another experiment, one group of 12 mice corresponding to a control group was injected with PBS, while a second group of 12 mice was immunized with formaldehyde killed whole cells of GBS strain C388/90 (Ia/c). Six mice from each of these two groups were challenged with 2.1×10^6 cfu of the GBS strain C388/90 (Ia/c) (Table I). As the first challenge experiment, all mice immunized with the GBS strain C388/90 (Ia/c) survived the homologous challenge.

Only two out of the 6 mice injected with PBS survived the infection.

The remaining 6 mice in both groups were then used one week later to verify whether this antigenic preparation could confer cross protection against strain NCS246 (II/R) which produce a serologically distinct capsule. None of the mice infected with this second GBS strain survived the infection. The later result suggested that most of the protective immune response induced by formaldehyde killed strain C388/90 is directed against the capsular polysaccharide and that it could be restricted to strains of that particular serotype. These results clearly indicated that this particular model of infection can be efficiently used to study the protection conferred by vaccination.

15

EXAMPLE 3 Immunization of rabbit with formaldehyde killed whole GBS cells and passive protection in mice

A New Zealand rabbit (2.5 kg, Charles River, St-Constant, Québec, Canada) was immunized with formaldehyde killed cells of GBS strain C388/90 (Ia/c) to obtain hyperimmune serum. This rabbit was injected subcutaneously three times at three weeks interval with approximately 1.5×10^9 cfu of formaldehyde killed whole cells of GBS strain C388/90 (Ia/c). Freund's complete adjuvant (Gibco BRL Life Technologies, Grand Island, New York) was used as the adjuvant for the first immunization, while Freund's incomplete adjuvant (Gibco BRL) was used for the following two injections. Serum samples were obtained before the beginning of the immunization protocol and two weeks after the last injection. The sera were frozen at -20°C.

The ability of this particular rabbit hyperimmune serum to passively protect mice against a lethal infection with GBS

was also evaluated. Intraperitoneal injection of mice with either 15 or 25 μ L of hyperimmune rabbit serum 18 hours before the challenge protected 4 out of 5 mice (80%) against the infection. Comparatively, survival rates lower than 20% 5 were recorded for mice in the control group injected with PBS or serum obtained from a rabbit immunized with meningococcal outer membrane preparation. This result clearly indicates that the immunization of another animal species with killed GBS cells can induce the production of 10 antibodies that can passively protect mice. This reagent will also be used to characterize clones.

15 Table 2 Passive protection of CD-1 mice conferred by rabbit serum obtained after immunization with formaldehyde killed group B whole streptococci (strain C388/90 (Ia/c)) antigenic preparation

groups	number of living mice 14 days after the bacterial challenge with GBS strain C388/90 (Ia/c) ²	% survival
rabbit hyperimmune serum ² - 25 μ l	4/5	80
rabbit hyperimmune serum ¹ - 15 μ l	4/5	80
control rabbit serum - 25 μ l	1/5	20
control PBS	1/10	10

20 ¹ Freund's complete adjuvant was used for first immunization, and Freund's incomplete adjuvant for the following two injections;

² intraperitoneal challenge with 1 ml Todd-Hewitt culture medium containing GBS C388/90 (Ia/c) suspension adjusted to 2×10^4 cfu.

25

EXAMPLE 4 Recombinant production of His.Tag-GBS fusion protein

The coding region of a GBS gene was amplified by PCR (DNA Thermal Cycler GeneAmp PCR system 2400 Perkin Elmer, San Jose, CA) from the genomic DNA of GBS strain C388/90 (Ia/c) using the oligos that contained base extensions for the addition of the restriction sites BglII (AGATCT) and HindIII (AAGCTT), respectively. The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and HindIII (Pharmacia Canada Inc Baie d'Urfe, Canada), and extracted with phenol:chloroform before ethanol precipitation. The pET-32b(+) vector (Novagen, Madison, WI) containing the thioredoxin-His.Tag sequence was digested with the restriction enzymes BglII and HindIII, extracted with phenol:chloroform, and then ethanol precipitated. The BglII-HindIII genomic DNA fragment was ligated to the BglII-HindIII pET-32b(+) vector to create the coding sequence for thioredoxin-His.Tag-GBS fusion protein whose gene was under control of the T7 promoter. The ligated products were transformed into *E. coli* strain XLI Blue MRF' ($\Delta(mcrA)183\Delta$ ($mcrCB-hsdSMR-mrr$)173 $endA1$ $supE44$ $thi-1$ $recA1$ $gyrA96$ $relA1$ lac [F'proAB $lacI^q$ Z $\Delta M15$ Tn10 (Tet^r)]^c) (Stratagene, La Jolla, CA) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D.M. Glover (ed.), pp. 109-135). The recombinant pET plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of the DNA insert was verified by DNA sequencing (Taq Dye Deoxy Terminator Cycle Sequencing kit, ABI, Foster City, CA). The recombinant pET plasmid was transformed by electroporation (Gene Pulser II apparatus, BIO-RAD Labs, Mississauga, Canada) into *E. coli* strain AD494 (DE3) (Δara^r $leu7697$ $\Delta lacX74$ $\Delta phoA$ $PvuII$ $phoR$ $\Delta malF3$ F' [lac^r(lacI^q) pro] *trxB*::Kan (DE3)) (Novagen, Madison, WI). In this strain of

E. coli, the T7 promoter controlling expression of the fusion protein, is specifically recognized by the T7 RNA polymerase (present on the λ DE3 prophage) whose gene is under the control of the lac promoter which is inducible by 5 isopropyl- β -D-thiogalactopyranoside (IPTG).

The transformant AD494(DE3)/rpET was grown at 37°C with agitation at 250 rpm in LB broth (peptone 10g/L, Yeast extract 5g/L, NaCl 10g/L) containing 100 μ g of ampicillin 10 (Sigma-Aldrich Canada Ltd., Oakville, Canada) per mL until the A_{600} reached a value of 0.6. In order to induce the production of the thioredoxin-His.Tag-GBS fusion protein, the cells were incubated for 2 additional hours in the presence of IPTG at a final concentration of 1mM. The 15 bacterial cells were harvested by centrifugation.

The recombinant fusion protein produced by AD494(DE3)/rpET32 upon IPTG induction for 2h was partially obtained as insoluble inclusion bodies which were purified from 20 endogenous E. coli proteins by the isolation of insoluble aggregates (Gerlach, G.F. et al 1992, Infect. Immun. 60:892). Induced cells from a 500 mL culture were resuspended in 20 mL of 25% sucrose-50mM Tris-HCl buffer (pH8.0) and frozen at -70°C. Lysis of cells in thawed 25 suspension was achieved by the addition of 5mL of a solution of lysozyme (10mg/mL) in 250mM Tris-HCl buffer (pH8.0) followed by an incubation of 10 to 15 min on ice, and the addition of 150mL of detergent mix (5 parts of 20mM Tris-HCl buffer [pH7.4]-300mM NaCl-2% deoxycholic acid-2% Nonidet P- 30 40 and 4 parts of 100mM Tris-HCl buffer [pH8]-50mM EDTA-2% Triton X-100) followed by 5 min incubation on ice. Upon sonication, protein aggregates were harvested by centrifugation for 30 min at 35,000 X g and a sample of the 35 soluble cellular fraction was kept. The aggregated proteins were solubilized in 6M guanidine hydrochloride. The

presence of the fusion protein in both the soluble and insoluble fractions was shown by Western Blot analysis using the serum of a mouse injected with formaldehyde killed cells of GBS strain C388/90 (Ia/c) that survived a bacterial challenge with the corresponding GBS strain.

The purification of the fusion protein from the soluble fraction of IPTG-induced AD494 (DE3) /rpET was done by affinity chromatography based on the properties of the His.Tag sequence (6 consecutive histidine residues) to bind to divalent cations (Ni^{2+}) immobilized on the His.Bind metal chelation resin (Novagen, Madison, WI). The purification method used are those described in the pET system Manual, 6th Edition (Novagen, Madison, WI). Briefly, the pelleted cells obtained from a 100mL culture induced with IPTG was resuspended in 4mL of Binding buffer (5mM imidazole-500mM NaCl-20mM Tris-HCl pH7.9), sonicated, and spun at 39,000 X g for 20 min to remove debris. The supernatant was filtered (0.45 μm pore size membrane) and deposited on a column of His.Bind resin equilibrated in Binding buffer. The column was then washed with 10 column volumes of Binding buffer followed by 6 column volumes of Wash buffer (20mM imidazole-500mM NaCl-20mM Tris-HCl pH7.9). The thioredoxin-His.Tag-GBS fusion protein was eluted with Elute buffer (1M imidazole-500mM NaCl-20mM Tris-HCl pH7.9). The removal of the salt and imidazole from the sample was done by dialysis against 3 X 1 liter PBS at 4°C.

The quantities of fusion protein obtained from either the soluble or insoluble cytoplasmic fractions of *E. coli* were estimated by Coomassie staining of a sodium dodecyl sulfate (SDS)-polyacrylamide gel with serial dilutions of these proteins and a bovine serum albumin standard (Pierce Chemical Co. Rockford, Ill.).

EXAMPLE 5 Recombinant production of GBS protein under control of lambda P. promoter

The DNA coding region of a GBS protein was inserted downstream of the promoter λP_L into the translation vector pURV22. This plasmid was derived from p629 (George et al, 1987, Bio/Technology 5:600) from which the coding region for a portion of the herpes simplex virus type I (HSV-I) glycoprotein (gD-1) was removed and the ampicillin resistance gene replaced by a kanamycin cassette obtained from the plasmid vector pUC4K (Pharmacia Biotech Canada Inc., Baie D'Urfe, Canada). The vector contained a cassette of the bacteriophage λ cI857 temperature sensitive repressor gene from which the functional P_R promoter had been deleted. The inactivation of the cI857 repressor by temperature increase from the ranges of 30-37°C to 37-42°C resulted in the induction of the gene under the control of λP_L . The translation of the gene was controlled by the ribosome binding site cro followed downstream by a BglII restriction site (AGATCT) and the ATG: ACTAAGGAGGTTAGATCTATG.

Restriction enzymes and T4 DNA ligase were used according to suppliers (Pharmacia Biotech Canada Inc., Baie D'Urfe, Canada; and New England Biolabs Ltd., Mississauga, Canada).
25 Agarose gel electrophoresis of DNA fragments was performed as described by Sambrook et al. (Molecular cloning : A laboratory Manual, 1989, Cold Spring Harbor Laboratory Press, N.Y). Chromosomal DNA of the GBS bacteria was prepared according to procedures described in Jayarao et al (J. Clin. Microbiol., 1991, 29:2774). DNA amplification reactions by polymerase chain reaction (PCR) were made using DNA Thermal Cycler GeneAmp PCR system 2400 (Perkin Elmer, San Jose, CA). Plasmids used for DNA sequencing were purified using plasmid kits from Qiagen (Chatsworth, CA).
30 35 DNA fragments were purified from agarose gels using Qiaex II

gel extraction kits from Qiagen (Chatsworth, CA). Plasmid transformations were carried out by the method described by Hanahan (DNA Cloning, Glover (ed.) pp, 109-135, 1985). The sequencing of genomic DNA inserts in plasmids was done using 5 synthetic oligonucleotides which were synthesized by oligonucleotide synthesizer model 394 (the Perkin-Elmer Corp., Applied Biosystems Div. (ABI), Foster City, CA). The sequencing reactions were carried out by PCR using the Taq Dye Deoxy Terminator Cycle Sequencing kit (ABI, Foster City, 10 CA) and DNA electrophoresis was performed on automated DNA sequencer 373A (ABI, Foster City, CA). The assembly of the DNA sequence was performed using the program Sequencer 3.0 (Gene Codes Corporation, Ann Arbor, MI). Analysis of the DNA sequences and their predicted polypeptides was performed 15 with the program Gene Works version 2.45 (Intelligenetics, Inc., Mountain View CA).

The coding region of the GBS gene was amplified by PCR from GBS strain C388/90 (Ia/c) genomic DNA using oligos that 20 contained base extensions for the addition of restriction sites BglII (AGATCT) and XbaI (TCTAGA), respectively. The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and XbaI, and extracted with 25 phenol:chloroform before ethanol precipitation. The pURV22 vector was digested with the restriction enzymes BglII and XbaI, extracted with phenol:chloroform, and ethanol precipitated. The BglII-XbaI genomic DNA fragment was ligated to the BglII-XbaI pURV22 vector in which the GBS 30 gene was under the control of the λ PL promoter. The ligated products were transformed into *E. coli* strain XLI Blue MRF' (Δ (*mcrA*) 183 Δ (*mcrCB-hsdSMR-mrr*) 173 *endA1 supE44 thi-1 recA1 gyrA96 relA1 lac* [F' *proAB lacI*^q Z Δ M15 *Tn10* (Tet^r)]^c) (Stratagene, La Jolla CA) according to the methods described 35 in Hanahan, supra. Transformants harboring plasmids with the

insert were identified by analysis of lysed cells submitted to electrophoresis on agarose gel (Sambrook et al, supra). The recombinant pURV22 plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of 5 the DNA insert was verified by DNA sequencing.

The transformant XLI Blue MRF'/rpURV22 was grown at 34°C with agitation at 250 rpm in LB broth containing 50µg of kanamycin per mL until the A_{600} reached a value of 0.6. In 10 order to induce the production of the fusion protein, the cells were incubated for 4 additional hours at 39°C. The bacterial cells were harvested by centrifugation, resuspended in sample buffer, boiled for 10 min and kept at -20°C.

15

EXAMPLE 6 Subcloning GBS protein gene in CMV plasmid pCMV-GH

The DNA coding region of a GBS protein was inserted in phase 20 downstream of the human growth hormone (hGH) gene which was under the transcriptional control of the cytomegalovirus (CMV) promoter in the plasmid vector pCMV-GH (Tang et al, Nature, 1992, 356:152). The CMV promoter is non functional in E. coli cells but active upon administration of the 25 plasmid in eukaryotic cells. The vector also incorporated the ampicillin resistance gene.

The coding region of the gene was amplified by PCR from 30 genomic DNA of GBS strain C388/90 (Ia/c) using the oligos that contained base extensions for the addition of the restriction sites BglII (AGATCT) and HindIII (AAGCTT). The PCR product was purified from agarose gel using a Qiaex II gel extraction kit from Qiagen (Chatsworth, CA), digested with the restriction enzymes BglII and HindIII, and 35 extracted with phenol:chloroform before ethanol precipitation. The pCMV-GH vector (Laboratory of Dr. Stephen

A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas) containing the human growth hormone to create fusion proteins was digested with the restriction enzymes BamHI and HindIII, extracted with phenol:chloroform, 5 and ethanol precipitated. The 1.3-kb BglII-HindIII genomic DNA fragment was ligated to the BamHI -HindIII pCMV-GH vector to create the hGH-GBS fusion protein under the control of the CMV promoter. The ligated products were transformed into *E. coli* strain DH5 α [φ80 lacZ ΔM15 endA1 10 recA1 hsdR17 (r K m K $^+$) supE44 thi-1λ $^+$ gyrA96 relA1 Δ(lacZYA- argF)U169] (Gibco BRL, Gaithersburg, MD) according to the methods described by Hanahan, supra. Transformants harboring plasmids with the insert were identified by analysis of lysed cells submitted to electrophoresis on 15 agarose gel (Sambrook, J. et al , supra). The recombinant pCMV plasmid was purified using a Qiagen kit (Qiagen, Chatsworth, CA) and the nucleotide sequence of the DNA insert was verified by DNA sequencing.

20

EXAMPLE 7 Immunological activity of GBS protein to GBS challenge

Four groups of 12 female CD-1 mice (Charles River, St- 25 Constant, Quebec, Canada) of 6 to 8 weeks were injected subcutaneously three times at three week intervals with 0.1mL of the following antigenic preparations: formaldehyde killed cells of GBS strain C388/90 (\sim 6X10 7 cfu), 20 μ g of thioredoxin-His.Tag-GBS fusion protein obtained from the 30 insoluble (inclusion bodies) or 20 μ g of the fusion protein, affinity purified (nickel column), from the soluble cytoplasmic fraction in *E.coli*, or 20 μ g of affinity purified (nickel column) thioredoxin-His.Tag control polypeptide. 20 μ g of QuilATM (Cedarlane Laboratories Ltd, Hornby, Canada)

was added to each antigenic preparation as the adjuvant. Serum samples were obtained from each mouse before immunization (PB) and on days 20 (TB1), 41 (TB2) and 54 (TB3) during the immunization protocols. Sera were frozen 5 at -20°C.

An increase of the ELISA titers was recorded after each injection of the fusion protein indicating a good primary response and a boost of the specific humoral immune response 10 after each of the second and third administration. At the end of the immunization period, the means of reciprocal ELISA titers was 456,145 for the group immunized with 20 μ g of fusion protein obtained from inclusion bodies compared to 290,133 for the group of mice immunized with the protein 15 from soluble fraction in *E.coli*. The latter result suggests that the protein obtained from inclusion bodies could be more immunogenic than the soluble protein. Analysis of mice sera in ELISA using the affinity purified thioredoxin-His.Tag to coat plates showed that negligible antibody 20 titers are made against the thioredoxin-His.Tag portion of the fusion protein. The reactivity of the sera from mice injected with the recombinant fusion protein was also tested by ELISA against formaldehyde killed whole cells of GBS strain C388/90. The antibodies induced by immunization with 25 recombinant fusion protein also recognized their specific epitopes on GBS cells indicating that their conformation is close enough to the native streptococcal protein to induce cross-reactive antibodies.

30 To verify whether the immune response induced by immunization could protect against GBS infection, mice were challenged with 3.5×10^5 cfu of GBS strains C338/90(Ia/c) and 1.2×10^5 cfu of strain NCS246(II/R) the results of which are illustrated in tables 3 and 4 respectively. Mice immunized 35 with control thioredoxin-His.Tag peptide were not protected against challenge with either GBS strain while those

immunized with formaldehyde killed C388/90 whole cells only provided protection against homologous challenge. The thioredoxin-His.Tag-GBS fusion protein of the invention protected mice from challenge with both GBS strains. Blood 5 and spleen culture of these mice did not reveal the presence of any GBS.

Table 3 Survival from GBS strain C388/90 (Ia/c) challenge¹

immunizing agent	no. mice surviving challenge	% survival
thioredoxin-His.Tag ²	1 / 6	17
formaldehyde killed C388/90 cells ³	6 / 6	100
thioredoxin-His.Tag-GBS fusion (inclusion body preparation) ⁴	6 / 6	100
thioredoxin-His.Tag-GBS fusion (cytoplasmic fraction) ⁴	6 / 6	100

¹ intraperitoneal administration with 1 ml Todd-Hewitt culture medium adjusted to 3.5×10^5 cfu;
 5 ² 20 μ g administered; posterior legs paralyzed in surviving mouse; GBS detected in blood and spleen;
³ 6×10^7 cfu administered;
⁴ 20 μ g administered.

Table 4 Survival from GBS strain NCS246 (II/R) challenge¹

immunizing agent	no. mice surviving challenge	% survival
thioredoxin-His.Tag ²	0 / 6	0
formaldehyde killed C388/90 cells ³	2 / 6	34
thioredoxin-His.Tag-GBS fusion (inclusion body preparation) ²	5 / 5 ⁴	100
thioredoxin-His.Tag-GBS fusion (cytoplasmic fraction) ²	6 / 6	100

5 ¹ intraperitoneal administration with 1 ml Todd-Hewitt culture medium containing GBS NCS246 (II/R) suspension adjusted to 1.2×10^5 cfu.

20 ² 20 μ g administered;

3 ³ 6×10^7 cfu administered;

10 ⁴ one mouse died during immunization.

EXAMPLE 8 Immunization with recombinant GBS protein confers protection against experimental GBS infection

15

This example illustrates the protection of mice against fatal GBS infection by immunization with the recombinant protein corresponding to the SEQ ID NO:39.

20 Groups of 10 female CD-1 mice (Charles River) were immunized subcutaneously three times at three-week intervals with 20 μ g of recombinant protein purified from E. coli strain BLR (Novagen) harboring the recombinant pURV22 plasmid vector containing the GBS gene corresponding to SEQ ID NO:42 in presence of 20 μ g of QuilATM adjuvant (Cedarlane Laboratories Ltd, Hornby, Canada) or, as control, with

QuilA™ adjuvant alone in PBS. Blood samples were collected from the orbital sinus on day 1, 22 and 43 prior to each immunization and fourteen days (day 57) following the third injection. One week later the mice were challenged with 5 approximately 10^4 to 10^6 CFU of various virulent GBS strains.

Samples of the GBS challenge inoculum were plated on TSA/5% sheep blood agar plates to determine the CFU and to verify the challenge dose. Deaths were recorded for a period of 14 days and on day 14 post-challenge, the surviving mice were 10 sacrificed and blood and spleen were tested for the presence of GBS organisms. The survival data are shown in table 5.

Prechallenge sera were analyzed for the presence of antibodies reactive with GBS by standard immunoassays. Elisa 15 and immunoblot analyses indicated that immunization with recombinant GBS protein produced in *E. coli* elicited antibodies reactive with both, recombinant and native GBS protein. Antibody responses to GBS are described in Example 9.

20

Table 5. Ability of recombinant GBS protein corresponding to SEQ ID NO: 39 to elicit protection against 8 diverse GBS challenge strains

5

		Challenge strain		
Immunogen	Designation	Type	No. alive:	No. dead ¹
rGBS protein none	C388/90	Ia/c	8 : 2 0 : 10	(P<0.0001)
rGBS protein none	NCS 246	II/R	10 : 0 3 : 7	(P=0.0012)
rGBS protein none	ATCC12401	Ib	10 : 0 3 : 7	(P=0.001)
rGBS protein none	NCS 535	V	10 : 0 5 : 5	(P=0.01)
rGBS protein none	NCS 9842	VI	10 : 0 0 : 10	(P<0.0001)
rGBS protein NCS 915-F ³ none	NCS 915	III	7 : 3 1 : 9 4 : 6	(P=0.0007) ²
rGBS protein NCS 954-F none	NCS 954	III/R	7 : 3 4 : 6 1 : 9	(P=0.002)
rGBS protein COH1-F none	COH1	III	4 : 6 3 : 7 0 : 10	(P=0.0004)

10 ¹ Groups of 10 mice per group were used, the number of mice surviving to infection and the number of dead mice are indicated. The survival curves corresponding to recombinant GBS protein-immunized animals were compared to the survival curves corresponding to mock-immunized animals using the log-rank test for nonparametric analysis.

² Comparison analysis to NCS915-F-immunized animals.

15 ³ Animals were immunized with formaldehyde-killed GBS in presence of QuilA™ adjuvant.

20 All hemocultures from surviving mice were negative at day 14 post-challenge. Spleen cultures from surviving mice were negative except for few mice from experiment MB-11.

EXAMPLE 9 Vaccination with the recombinant GBS protein elicits an immune response to GBS

Groups of 10 female CD-1 mice were immunized subcutaneously
5 with recombinant GBS protein corresponding to SEQ ID NO:39
as described in Example 8. In order to assess the antibody
response to native GBS protein, sera from blood samples
collected prior each immunization and fourteen days after
the third immunization were tested for antibody reactive
10 with GBS cells by ELISA using plates coated with
formaldehyde-killed GBS cells from type III strain NCS 954,
type Ib strain ATCC12401, type V strain NCS 535 or type VI
strain NCS 9842. The specificity of the raised antibodies
15 for GBS protein was confirmed by Western blot analyses to
GBS cell extracts and purified recombinant antigens. The
results shown in Figure 10 clearly demonstrate that animals
respond strongly to recombinant GBS protein used as
immunogens with median reciprocal antibody titers varying
between 12000 and 128000, for sera collected after the third
20 immunization, depending of the coating antigen. All
preimmune sera were negative when tested at a dilution of
1 :100. GBS-reactive antibodies were detectable in the sera
of each animal after a single injection of recombinant GBS
protein.

25

Example 10 Antigenic conservation of the GBS protein of the present invention

5 Monoclonal antibodies (MAbs) specific to the GBS protein of the present invention were used to demonstrate that this surface antigen is produced by all GBS and that it is also antigenically highly conserved.

10 A collection of 68 GBS isolates was used to evaluate the reactivity of the GBS-specific MAbs. These strains were obtained from the National Center for Streptococcus, Provincial Laboratory of Public Health for Northern Alberta, Canada; Centre Hospitalier Universitaire de Quebec, Pavillon CHUL, Quebec, Canada; American Type Culture Collection, USA; 15 Laboratoire de Sante Publique du Quebec, Canada; and Dept. of Infectious Disease, Children's Hospital and Medical Center, Seattle, USA. All eight MAbs were tested against the following panel of strains: 6 isolates of serotype Ia or Ia/c, 3 isolates of serotype Ib, 4 isolates of serotype II, 20 14 isolates of serotype III, 2 isolates of serotype IV, 2 isolates of serotype V, 2 isolates of serotype VI, 2 isolates of serotype VII, 1 isolate of serotype VIII, 10 isolates that were not serotyped and 3 bovine *S. agalactiae* strains. MAb 3A2 was also reacted with additional GBS: 9 isolates of serotype Ia/c and 10 isolates of serotype V. The strains were grown overnight on blood agar plates at 37°C in an atmosphere of 5% CO₂. Cultures were stored at - 25 70°C in heart infusion broth with 20% (v/v) glycerol.

30 To obtain the GBS protein-specific MAbs, mice were immunized three times at three-week intervals with 20 µg of purified recombinant GBS protein (SEQ ID NO :44) in the presence of 20% QuilA™ adjuvant. Hybridoma cell lines were generated by fusion of spleen cells recovered from immunized mice with 35 the nonsecreting SP2/0 myeloma cell line as described

previously (Hamel, J. et al. 1987. J. Med. Microbiol. 23:163-170). Hybrid clone supernatants were tested for specific antibody production by ELISA using formaldehyde inactivated GBS and purified recombinant GBS protein (SEQ ID NO :39 or 44) as coating antigen, as previously described (Hamel, J. et al. 1987. J. Med. Microbiol. 23:163-170). Specific hybrid were cloned by limiting dilutions, expanded, and frozen in liquid nitrogen. Production of recombinant GBS protein was presented in Examples 4 & 5. Purified recombinant GBS protein or formaldehyde inactivated GBS were resolved by electrophoresis by using the discontinuous buffer system of Laemmli as recommended by the manufacturer and then transfer onto nitrocellulose membrane for Western immunoblotting as described previously (Martin et al. 1992. Infect. Immun. 60:2718-2725).

Western immunoblotting experiments clearly indicated that all eight MAbs recognized a protein band that corresponded to the purified recombinant GBS protein (SEQ ID NO :39). These MAbs also reacted with a protein band present in every GBS isolates tested so far. The reactivity of these GBS-specific MAbs are presented in Table 6. Each MAb reacted well with all 46 GBS. In addition, these MAbs also recognized the 3 *S. agalactiae* strains of bovine origin that were tested. MAb 3A2 also recognized nineteen GBS; 9 isolates of serotype Ia/c and 10 of serotype V. The other MAbs were not tested against these additional strains.

These results demonstrated that the GBS protein (SEQ ID NO :39) was produced by all the 65 GBS and the three 3 *S. agalactiae* strains of bovine origin that were tested so far. More importantly, these results clearly demonstrated that the epitopes recognized by these eight GBS-specific MAbs were widely distributed and conserved among GBS. These results also indicated that these epitopes were not

restricted to serologically related isolates since representatives of all known GBS serotypes including the major disease causing groups were tested.

- 5 In conclusion, the data presented in this example clearly demonstrated that the GBS protein of the present invention is produced by all GBS and that it is antigenically highly conserved.

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Table 6. Reactivity of eight GBS protein-specific MAbs with different *S. agalactiae* strains as evaluated by Western immunoblots.

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Mabs	Number of each serotype of <i>S. agalactiae</i> strains recognized by the MAbs.										Bovine (3)
	Ia or Ia/c (6)	Ib (3)	II (4)	III (4)	IV (2)	V (2)	VI (2)	VII (1)	VIII (1)	NT (10) 2	
3A21	6	3	4	4	2	2	2	1	10	46	3
5A12	6	3	4	4	2	2	2	1	10	46	3
6G11	6	3	4	4	2	2	2	1	10	46	2
8B9	6	3	4	4	2	2	2	1	10	46	3
8E11	6	3	4	4	2	2	2	1	10	46	3
12B12	6	3	4	4	2	2	2	1	10	46	3
18F11	6	3	4	4	2	2	2	1	10	46	3
20G2	6	3	4	4	2	2	2	1	10	46	3

1 Nine additional strains of serotype Ia/c and 10 strains of serotype V were recognized by MAb 3A2.

2 These strains were not serotyped

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WE CLAIM:

1. An isolated polynucleotide encoding a polypeptide having at least 70% identity to a second polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10,
SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15,
SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19,
SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24,
SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 29,
SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34,
SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 39,
SEQ ID NO: 40, SEQ ID NO: 41 and SEQ ID NO: 44 or
fragments, analogs or derivatives thereof.
2. A polynucleotide according to claim 1, wherein said polynucleotide encodes a polypeptide having at least 95% identity to the second polypeptide.
3. An isolated polynucleotide encoding a polypeptide capable of generating antibodies having binding specificity for a polypeptide having a sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10,
SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 15,
SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19,
SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 24,
SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 29,
SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 34,
SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 39,
SEQ ID NO: 40, SEQ ID NO: 41 and SEQ ID NO: 44 or
fragments, analogs or derivatives thereof.

4. An isolated polynucleotide that is complementary to the polynucleotide of claim 1.
5. An isolated polynucleotide that is complementary to the polynucleotide of claim 3.
6. The polynucleotide of claim 1, wherein said polynucleotide is DNA.
7. The polynucleotide of claim 3, wherein said polynucleotide is DNA.
8. The polynucleotide of claim 1, wherein said polynucleotide is RNA.
9. The polynucleotide of claim 3, wherein said polynucleotide is RNA.
10. A polynucleotide which hybridizes under stringent conditions to a second polynucleotide having a sequence selected from the group consisting of :
SEQ ID NO : 1, SEQ ID NO : 7, SEQ ID NO : 13, SEQ ID NO : 22, SEQ ID NO : 27, SEQ ID NO : 32, SEQ ID NO : 37, SEQ ID NO : 42 and SEQ ID NO : 43 or fragments, analogues or derivatives thereof.
11. A polynucleotide which hybridizes under stringent conditions to a second polynucleotide having a sequence selected from the group consisting of :
SEQ ID NO : 37, SEQ ID NO : 42 and SEQ ID NO : 43.
12. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 37.

13. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 42.
14. A polynucleotide according to claim 11 which hybridizes under stringent conditions to a second polynucleotide having the sequence SEQ ID NO : 43.
15. A polynucleotide according to claim 10 wherein said polynucleotide has at least 95% complementarity to the second polynucleotide.
16. A polynucleotide according to claim 11 wherein said polynucleotide has at least 95% complementarity to the second polynucleotide.
17. A vector comprising the polynucleotide of claim 1, wherein said polynucleotide is operably linked to an expression control region.
18. A vector comprising the polynucleotide of claim 3, wherein said polynucleotide is operably linked to an expression control region.
19. A host cell transfected with the vector of claim 17.
20. A host cell transfected with the vector of claim 18.
21. A process for producing a polypeptide comprising culturing a host cell according to claim 19 under conditions suitable for expression of said polypeptide.
22. A process for producing a polypeptide comprising culturing a host cell according to claim 20 under condition suitable for expression of said polypeptide.

23. An isolated polypeptide having at least 70% identity to a second polypeptide having a sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments, analogs or derivatives thereof.

24. The isolated polypeptide of claim 23 having a sequence according to SEQ ID NO : 39.

25. The isolated polypeptide of claim 23 having a sequence according to SEQ ID NO : 44.

26. An isolated polypeptide capable of generating antibodies having binding specificity for a second polypeptide having a sequence selected from the group consisting of:

SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41 and SEQ ID NO:44 or fragments, analogs or derivatives thereof.

27. The isolated polypeptide of claim 26 having a sequence according to SEQ ID NO : 39.
28. The isolated polypeptide of claim 26 having a sequence according to SEQ ID NO : 44.
29. An isolated polypeptide having an amino acid sequence selected from the group consisting of:
SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5,
SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO:10,
SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:15,
SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19,
SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:24,
SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:29,
SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34,
SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:39,
SEQ ID NO:40 and SEQ ID NO:41 or fragments, analogs or derivatives thereof.
30. The isolated polypeptide of claim 29 having an amino acid sequence according to SEQ ID NO : 39.
31. An isolated polypeptide having an amino acid sequence according to SEQ ID NO : 44.
32. An isolated polypeptide according to any one of claims 29 to 31, wherein the N-terminal Met residue is deleted.
33. An isolated polypeptide according to any one of claims 29 to 30, wherein the secretory amino acid sequence is deleted.
34. A vaccine composition comprising a polypeptide according to any one of claims 23 to 31 and a pharmaceutically acceptable carrier, diluent or adjuvant.

35. A vaccine composition comprising a polypeptide according to claim 32 and a pharmaceutically acceptable carrier, diluent or adjuvant.
36. A vaccine composition comprising a polypeptide according to claim 33 and a pharmaceutically acceptable carrier, diluent or adjuvant.
37. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 34.
38. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 35.
39. A method for therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of a composition according to claim 36.
40. A method according to any one of claims 37 to 39, wherein said animal is a bovine.
41. A method according to any one of claims 37 to 39, wherein said animal is a human.

42. A method according to any one of claims 37 to 39, wherein said bacterial infection is selected from the group consisting of group A streptococcus and group B streptococcus.
43. A method according to claim 42, wherein said bacterial infection is group B streptococcus.
44. Use of a vaccine composition according to claim 34 for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to or infected with streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
45. Use of a vaccine composition according to any one of claims 35 to 36 for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to or infected with streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
46. Use of a vaccine composition according to any one of claims 23 to 31 for the manufacture of a vaccine for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.
47. Use of a vaccine composition according to claim 32 for the manufacture of a vaccine for the therapeutic or

prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.

48. Use of a vaccine composition according to claim 33 for the manufacture of a vaccine for the therapeutic or prophylactic treatment of streptococcal bacterial infection in an animal susceptible to streptococcal infection comprising administering to said animal a therapeutic or prophylactic amount of the composition.

TATCTGGCAA AGAGCCAGCT AATCGTTTA GTTGGGCTAA AAATAAAATTA TTAATCAATG S G K E P A N R F S W A K N K L L I N G	60
----->	
GATTCAATTGC AACTCTAGCA GCAACTATCT TATTTTTGAGTTCAATTCAATTC ATAGGTCTTA F I A T L A A T I L F F A V Q F I G L K	120
AACCAGATTA CCCTGGAAAA ACCTACTTTA TTATCCTATT GACAGCATGG ACTTTGATGG P D Y P G K T Y F I I L L T A W T L M A	180
CATTAGTAAC TGCTTTAGTG GGATGGGATA ATAGGTATGG TTCCCTCTTG TCGTTATTAA L V T A L V G W D N R Y G S F L S L L I	240
TATTATTATT CCAGCTTGGT TCAAGCGCAG GAACTTACCC AATAGAATTG AGTCCTAAGT L L F Q L G S S A G T Y P I E L S P K F	300
TCTTCAAAC AATTCAACCA TTTTACCGA TGACTTACTC TGTTTCAGGA TTAAGAGAGA F Q T I Q P F L P M T Y S V S G L R E T	360
CCATCTCGTT GACGGGAGAC GTTAACCATC AATGGAGAAT GCTAGTAATC TTTTGTAT I S L T G D V N H Q W R M L V I F L V S	420
CATCGATGAT ACTTGCTCTT CTTATTTATC GTAAACAAGA AGATTAATAG AAAGTATCTA S M I L A L L I Y R K Q E D	480
GTGATAGACT AACAGTATGA TATGGTATGT CAAAGTATTG AGGAGGAGAA GATATGTCTA M S T ----->	540
CTTTAACAAAT AATTATTGCA ACATTAAC TG CTTGGAAACA TTTTATATT ATGTATTG L T I I I A T L T A L E H F Y I M Y L E	600
AGACGTTAGC CACCCAGTC AATATGACTG GGAAGATTG TAGTATGTCT AAAGAAGAGT T L A T Q S N M T G K I F S M S K E E L	660
TGTCATATTT ACCCGTTATT AAACTTTTA AGAATCAAGG TG TATAACAC GGCTTGATTG S Y L P V I K L F K N Q G V Y N G L I G	720
GCCTATTCCCT CCTTATGGG TTATATATT CACAGAATCA AGAAATTGTA GCTGTTTTT L F L L Y G L Y I S Q N Q E I V A V F L	780
TAATCAATGT ATTGCTAGTT GCTATTTATG GTGCTTGAC AGTTGATAAA AAAATCTTAT I N V L L V A I Y G A L T V D K K I L L	840
TAAAACAGGG TGGTTTACCT ATATTAGCTC TTTAACATT CTTATTTAA TACTACTTAG K Q G G L P I L A L L T F L F	900
CCGTTCGATT TAGTTGAACG GCTTTAGTA ATCATTTTT TCTCATAATA CAGGTAGTT AAGTAATTG TCTTAAAAAA TAGTATAATA TAACTACGAA TTCAAAGAGA GGTGACTTTG	960
ATTATGACTG AGAACTGGTT ACATACTAAA GATGGTTCAAG ATATTTATTA TCGTGTGTT M T E N W L H T K D G S D I Y Y R V V ----->	1020
GGTCAAGGTC AACCGATTGT TTTTTACAT GGCAATAGCT TAAGTAGTCG CTATTTGAT G Q G Q P I V F L H G N S L S S R Y F D	1080
AAGCAAATAG CATATTTTC TAAGTATTAC CAAGTTATTG TTATGGATAG TAGAGGGCAT K Q I A Y F S K Y Y Q V I V M D S R G H	1140
GGCAAAAGTC ATGCAAAGCT AAATACCATT AGTTTCAGGC AAATAGCAGT TGACTTAAAG G K S H A K L N T I S F R Q I A V D L K	1200
	1260

GATATCTTAG	TTCATTTAGA	GATTGATAAA	GTTATATTGG	TAGGCCATAG	CGATGGTGC	1320
D I L V	H L E	I D K	V I L V	G H S	D G A	
AATTTAGCTT	TAGTTTTCA	AACGATGTT	CCAGGTATGG	TTAGAGGGCT	TTTGCTTAAT	1380
N L A L	V F Q	T M F	P G M V	R G L	L L N	
TCAGGGAAACC	TGACTATTCA	TGGTCAGCGA	TGGTGGGATA	TTCTTTAGT	AAGGATTGCC	1440
S G N L	T I H	G Q R	W W D I	L L V	R I A	
TATAAATTCC	TTCACTATTT	AGGGAAACTC	TTTCCGTATA	TGAGGCAGAA	AGCTCAAGTT	1500
Y K F L	H Y L	G K L	F P Y M	R Q K	A Q V	
ATTTCGCTTA	TGTTGGAGGA	TTTGAAGATT	AGTCCAGCTG	ATTTACAGCA	TGTGTCAACT	1560
I S L M	L E D	L K I	S P A D	L Q H	V S T	
CCTGTAATGG	TTTGGTTGG	AAATAAGGAC	ATAATTAAGT	TAAATCATT	TAAGAAACTT	1620
P V M V	L V G	N K D	I I K L	N H S	K K L	
GCTCTTATT	TTCCAAGGGG	GGAGTTTAT	TCTTAGTTG	GCTTGGGCA	TCACATTATT	1680
A S Y F	P R G	E F Y	S L V G	F G H	H I I	
AAGCAAGATT	CCCATGTTT	TAATATTATT	GCAAAAAAAGT	TTATCAACGA	TACGTTGAAA	1740
K Q D S	H V F	N I I	A K K F	I N D	T L K	
GGAGAAAATTG	TTGAAAAAGC	TAATTGAAAA	AGTCAAATCA	CTGACTTCTG	TGATTAAT	1800
G E I V	E K A	N				
TGTATTTTT	ATATCTGTTT	TAGTGCTTAT	TATTGTTGAA	ATGATTCA	TGAAACGAAC	1860
				M I H L	K R T	
				----->		
TATTTCTGTT	GAGCAACTAA	AGAGTGT	TGGGCAATTA	TCTCCAATGA	ATCTTTCTT	1920
I S V	E Q L K	S V F	G Q L	S P M N	L F L	
AATTATCCTT	GTGGGGTTA	TCGCTGTCTT	ACCGACAACC	GGATATGACT	TTGTACTGAA	1980
I I L	V G V	I A V L	P T T	G Y D F	V L N	
TGGACTTTA	CGTACAGATA	AAAGCAAAAG	GTATATT	CAGACTAGTT	GGTGTATCAA	2040
G L L R	T D K S	K R Y	I L Q	T S W C	I N	
CACTTTAAT	AACTTGTCA	GATTGGTGG	CTTAATCGAT	ATTGGGTTGC	GCATGGCTT	2100
T F N N	L S G F	G G L	I D I	G L R M	A F	
TTATGGTAAA	AAAGGTCAAG	AGAAGAGTGA	CCTAAGAGAA	GTGACTCGTT	TTTTACCTA	2160
Y G K K	G Q E K	S D L	R E V	T R F L	P Y	
TCTTATTCT	GGTCTGTCA	TTATTAGTGT	GATTGCCTTA	ATCATGAGCC	ATATTTCA	2220
L I S G	L S F I	S V I	A L I	M S H I	F H	
TGCCAAAGCT	AGTGGTGT	ACTATTATTT	GGTATTAATT	GGTGTCTAGTA	TGTATTTCC	2280
A K A S	V D Y Y	Y L V	L I G	A S M Y	F P	
TGTTATTAT	TGGATTCTG	GTCATAAAGG	AAGCCATTAT	TTGGGAGATA	TGCCATCTAG	2340
V I Y W	I S G H	K G S	H Y F	G D M P	S S	
TACTCGTATA	AAATTAGGTG	TTGTTCTT	TTTGATGG	GGATGTGCGG	CCGCAGCATT	2400
T R I K	L G V V	S F F	E W G	C A A A	A F	
TATAATTATC	GGTTATTAA	TGGGCATTCA	TCTACCAGTT	TATAAAATT	TACCACTATT	2460
I I I G	Y L M G	I H L	P V Y	K I L P	L F	

TTGTATTGGT TGTGCCGTCG GGATTGTATC CCTTATTCCC GGTGGATTAG GAAGTTTGA 2520
 C I G C A V G I V S L I P G G L G S F E

 ATTAGTTCTA TTTACAGGGT TTGCTGCCGA GGGACTACCT AAAGAAACTG TGGTTGCATG 2580
 L V L F T G F A A E G L P K E T V V A W

 GTTATTACTT TATCGTTAG CCTACTATAT TATTCCATTTC TTTGCAGGTA TCTATTCTT 2640
 L L L Y R L A Y Y I I P F F A G I Y F F

 TATCCATTAT TTAGGTAGTC AAATAAAATCA ACGTTATGAA AATGTCCCGA AAGAGTTAGT 2700
 I H Y L G S Q I N Q R Y E N V P K E L V

 ATCAAATGTT CTACAAACCA TGGTGAGCCA TTTGATGCGT ATTTAGGTG CATTCTTAAT 2760
 S T V L Q T M V S H L M R I L G A F L I
 |---->

 ATTTCAACA GCATTTTTTG AAAATATTAC TTATATTATG TGGTTGCAGA AGCTAGGCTT 2820
 F S T A F F E N I T Y I M W L Q K L G L

 GGACCCATTA CAAGAACAAA TGTTATGGCA GTTTCCAGGT TTATTGCTGG GGGTTTGT 2880
 D P L Q E Q M L W Q F P G L L L G V C F

 TATTCTCTTA GCTAGAACTA TTGATCAAAA AGTGAAAAAT GCTTTCCAA TTGCTATTAT 2940
 I L L A R T I D Q K V K N A F P I A I I

 CTGGATTACT TTGACATTGT TTTATCTTAA TTTAGGTCAT ATTAGTTGGC GACTATCTT 3000
 W I T L T L F Y L N L G H I S W R L S F

 CTGGTTTATT TTACTATTGT TAGGCTTATT AGTCATTAAG CCAACTCTCT ATAAAAAAC 3060
 W F I L L L G L L V I K P T L Y K K Q

 ATTTATTTAT AGCTGGGAAG AGCGTATTAA GGATGGAATC ATTATCGTTA GTTTAATGGG 3120
 F I Y S W E E R I K D G I I I V S L M G

 AGTTCTATTT TATATTGCAG GACTACTATT CCCTATCAGG GCTCATATTA CAGGTGGTAG 3180
 V L F Y I A G L L F P I R A H I T G G S

 TATTGAACGC CTGCATTATA TCATAGCATG GGAGCCGATA GCATTGGCTA CGTTGATTCT 3240
 I E R L H Y I I A W E P I A L A T L I L

 TACTCTCGTT TATTTATGTT TGGTTAAGAT TTTACAAGGA AAATCTTGTG AGATTGGTGA 3300
 T L V Y L C L V K I L Q G K S C Q I G D

 TGTGTTCAAT GTGGATCGTT ATAAAAAAACT ACTTCAAGCT TACGGTGGTT CTTGGATAG 3360
 V F N V D R Y K K L L Q A Y G G S S D S

 CGGTTTAGCC TTTTAAATG ATAAAAGGCT CTACTGGTAC CAAAAAAATG GAGAAGATTG 3420
 G L A F L N D K R L Y W Y Q K N G E D C

 CGTTGCGTTC CAATTGTAA TTGTCATAA TAAATGTCTT ATTATGGGG AACCAAGCCGG 3480
 V A F Q F V I V N N K C L I M G E P A G

 TGATGACACT TATATTCGTG AAGCTATTGA ATCGTTTATT GATGATGCTG ATAAGCTAGA 3540
 D D T Y I R E A I E S F I D D A D K L D

 CTATGACCTT GTTTTTACA GTATTGGACA GAAGTTGACA CTACTTTAC ATGAGTATGG 3600
 Y D L V F Y S I G Q K L T L L H E Y G

 TTTGACTTT ATGAAAGTTG GTGAGGATGC TTTAGTTAAT TTAGAAACGT TTACTCTTAA 3660
 F D F M K V G E D A L V N L E T F T L K

AGGGAATAAG TACAAACCTT TCAGAAATGC CCTAAATAGA GTTGAAAAGG ATGGTTCTA	3720
G N K Y K P F R N A L N R V E K D G F Y	
TTTCGAAGTT GTACAATCGC CACATAGTCA AGAGCTACTA AATAGTTGG AAGAGATTC	3780
F E V V Q S P H S Q E L L N S L E E I S	
TAATACTTGG TTAGAAGGAC GTCCTGAAAA AGGTTCTCA CTAGGATATT TTAATAAAGA	3840
N T W L E G R P E K G F S L G Y F N K D	
TTATTTCCAA CAAGCCCCAA TAGCTTGTT AAAAAATGCT GAACACGAAG TTGTTGCTTT	3900
Y F Q Q A P I A L V K N A E H E V V A F	
TGCTAATATT ATGCCAAACT ATGAAAAGAG TATTATCTCT ATTGATTTAA TGCACGAGA	3960
A N I M P N Y E K S I I S I D L M R H D	
TAAACAGAAA ATTCCGAATG GCGTTATGGA TTTCCTCTT TTATCATTAT TCTCTTATTA	4020
K Q K I P N G V M D F L F L S L F S Y Y	
TCAAGAGAAG GGATACCACT ATTTTGATTT GGGGATGGCA CCTTTATCAG GAGTTGGTCG	4080
Q E K G Y H Y F D L G M A P L S G V G R	
CGTTGAAACA AGTTTGCTA AAGAGAGAAT GGCATATCTT GTCTATCATT TCGGTAGTCA	4140
V E T S F A K E R M A Y L V Y H F G S H	
TTTCTACTCA TTTAATGGTT TACACAAGTA TAAGAAGAAG TTTACACCATT GTGGTCGGA	4200
F Y S F N G L H K Y K K K F T P L W S E	
ACGTTATATT TCTTGTTCTC GTTCGTCTG GTTAATTGT GCTATTGTG CCCTATTAAT	4260
R Y I S C S R S S W L I C A I C A L L M	
GGAAGATAGT AAAATTAAGA TTGTTAAATA AGCTTTATTT GGCAATTAAA AAGAGCATGT	4320
E D S K I K I V K	
CATGCGACAT GCTCTTTA AATCATTAA TACCATGAT TGCTTGAATC TACTTTATAA	4380
TATGATGTGC TTTAAATAT TGTTTAGCTA CTGTAGCTGC TGATTTATGC TTTACAGCTA	4440
CTTGGTAGTT CATTCTTGC ATTTCTTTT CAGTGATATG ACCAGCAAGT TTATTGAGAG	4500
CTTTTTTAC TTGA (SEQ ID NO:1)	4514

FIG. 1a
[clone1-dna/aa]

SGKEPANRFS WAKNKLLING FIATLAATIL FFAVQFIGLK PDYPGKTYFI 50
ILLTAWTLMA LVTALVGWDN RYGSFLSLLI LLFQLGSSAG TYPIELSPKF 100
FQTIQPFLPM TYSVSGLRET ISLTGDVNHQ WRMLVIFLVS SMILALLIYR 150
KQED (SEQ ID NO:2) 154

FIG. 1b

MSTLTIIIAT LTALEHFYIM YLETLATQSN MTGKIFSMSK EELSYLPVIK 50
LFKNQGVYNG LIGLFLLYGL YISQNQEIVA VFLINVLLVA IYGALTVDKK 100
ILLKQGGLPI LALLTFLF (SEQ ID NO:3) 118

FIG. 1c

MTENWLHTKD GSDIYYRVVG QGQPIVFLHG NSLSSRYFDK QIAYFSKYYQ 50
VIVMDSRGHG KSHAKLNTIS FRQIAVDLKD ILVHLEIDKV ILVGHSDGAN 100
LALVFQTMFP GMVRGLLLNS GNLTIHGQRW WDILLVRIAY KFLHYLGKLF 150
PYMRQKAQVI SLMLEDLKIS PADLQHVSTP VMVLVGNKDI IKLNHSKKLA 200
SYFPRGEFYS LVGFHHIIK QDSHVFNIIA KKFINDTLKG EIVEKAN 247
(SEQ ID NO:4)

FIG. 1d

MIHLKRTISV	EQLKSVFGQL	SPMNLFLIIL	VGVIAVLPTT	GYDFVLNGLL	50
RTDKSKRYIL	QTSWCINTFN	NLSGFGLID	IGLRMAFYGK	KGQEKSDLRE	100
VTRFLPYLIS	GLSFISVIAL	IMSHIFHAKA	SVDYYYLVLI	GASMYFPVIY	150
WISGHKGSHY	FGDMPSSSTRI	KLGVVSSFEW	GCAAAAFIII	GYLMGIHLPV	200
YKILPLFCIG	CAVGIVSLIP	GGLGSFELVL	FTGFAAEGLP	KETVVAWLLL	250
YRLAYYIIPF	FAGIYFFIHY	LGSQINQRYE	NVPKELVSTV	LQTMVSHLMR	300
ILGAFLIFST	AFFENITYIM	WLQKLGLDPL	QEQMLWQFPG	LLLGVCFILL	350
ARTIDQKVKN	AFPIAIIWIT	LTLFYLNLGH	ISWRSLFWFI	LLLLGLLVIK	400
PTLYKKQFIY	SWEERIKDGI	IIVSLMGVLF	YIAGLLFPIR	AHITGGSIER	450
LHYIIIAWEPI	ALATLILTLV	YLCLVKILQG	KSCQIGDVFN	VDRYKKLLQA	500
YGGSSDGLA	FLNDKRLYWY	QKNGEDCVAF	QFVIVNNKCL	IMGEPAGDDT	550
YIREAIESFI	DDADKLDYDL	VFYSIGQKLT	LLLHEYGFDF	MKVGEDALVN	600
LETFTLKGNK	YKPFRNALNR	VEKDGFYFEV	VQSPHSQELL	NSLEEISNTW	650
LEGRPEKGFS	LGYFNKDYFQ	QAPIALVKNA	EHEVVAFANI	MPNYEKSIIS	700
IDLMRHDKQK	IPNGVMDLF	LSLFSYQEK	GYHYFDLGMA	PLSGVGRVET	750
SFAKERMAYL	VYHFGSHFYS	FNGLHKYKKK	FTPLWSERYI	SCSRSSWLIC	800
AICALLMEDS	KIKIVK	(SEQ ID NO:5)			816

FIG. 1e

MRILGAFLIF	STAFFENITY	IMWLQKLGLD	PLQEQMLWQF	PGLLLGVCFI	50
LLARTIDQKV	KNAFPIAIW	ITLTLFYLNL	GHISWRSLFW	FILLLLGLLV	100
IKPTLYKKQF	IYSWEERIKD	GIIIVSLMGV	LFYIAGLLFP	IRAHITGGSI	150
ERLHYIIIAWE	PIALATLILT	LVYLCLVKIL	QGKSCQIGDV	FNVDRYKKLL	200
QAYGGSSDGS	LAFLNDKRLY	WYQKNGEDCV	AFQFVIVNNK	CLIMGEPAGD	250
DTYIREAIES	FIDDADKLDY	DLVFYSIGQK	LTLLLHEYGF	DFMKVGEDAL	300
VNLETFTLKG	NKYKPFRNAL	NRVEKDGFYF	EVVQSPHSQE	LLNSLEEISN	350
TWLEGRPEKG	FSLGYFNKDY	FQQAPIALVK	NAEHEVVAFA	NIMPNEYEKSI	400
ISIDLMRHDK	QKIPNGVMDF	LFLSLFSYYQ	EKGYHYFDLG	MAPLSGVGRV	450
ETSFAKERMA	YLVYHFGSHF	YSFNGLHKYK	KKFTPLWSER	YISCSRSSL	500
ICAICALLME	DSKIKIVK	(SEQ ID NO:6)			518

FIG. 1f

AATTTGATA	TCGAAACAAAC	AACTTTGAG	GCAATGAAAAA	AGCACCGTC	ATTATTGGAG	60
N F D I	E T T	T F E	A M K K	H A S	L L E	
----->						
AAAATATCTG	TTGAGCGTTC	TTTATTGAA	TTTGATAAAC	TTCTATTAGC	ACCTTATTGG	120
K I S V	E R S	F I E	F D K L	L L A	P Y W	
CGTAAAGGAA	TGCTGGCACT	AATAGATAGT	CATGCTTTA	ATTATCTACC	ATGCTTAAAAA	180
R K G M	L A L	I D S	H A F N	Y L P	C L K	
AATAGGAAAT	TACAATTAAG	CGCCTTTTG	TCCCAGTTAG	ATAAAGATTT	TTTATTGAG	240
N R E L	Q L S	A F L	S Q L D	K D F	L F E	
ACATCAGAAC	AAGCTTGGGC	ATCACTCATC	TTGAGTATGG	AAGTTGAACA	CACAAAGACT	300
T S E Q	A W A	S L I	L S M E	V E H	T K T	
TTTTAAAAAA	AATGGAAGAC	ATCAACTCAC	TTTCAAAAAG	ATGTTGAGCA	TATAGTGGAT	360
F L K K	W K T	S T H	F Q K D	V E H	I V D	
GT TTATCGTA	TTCGTGAACA	AATGGGATTG	GCTAAAGAAC	ATCTTTATCG	TTATGGAAAAA	420
V Y R I	R E Q	M G L	A K E H	L Y R	Y G K	
ACTATAATAA	AACAAGCGGA	AGGTATT CGC	AAAGCAAGAG	GCTTGATGGT	TGATTTCGAA	480
T I I K	Q A E	G I R	K A R G	L M V	D F E	
AAAATAGAAC	AACTAGATAG	TGAGTTAGCA	ATCCATGATA	GGCATGAGAT	AGTTGTCAAT	540
K I E Q	L D S	E L A	I H D R	H E I	V V N	
GGTGGCACCT	TAATCAAGAA	ATTAGGAATA	AAACCTGGTC	CACAGATGGG	AGATATTATC	600
G G T L	I K K	L G I	K P G P	Q M G	D I I	
TCTCAAATTG	AATTAGCCAT	TGTTTTAGGA	CAACTGATTA	ATGAAGAAGA	GGCTATT TTA	660
S Q I E	L A I	V L G	Q L I N	E E E	A I L	
CATTTGTTA	AGCAGTACTT	GATGGATTAG	AGAGGATTAT	ATGAGCGATT	TTTTAGTAGA	720
H F V K	Q Y L	M D		M S D F	L V D	
----->						
TGGATTGACT	AAGTCGGTTG	GTGATAAGAC	GGTCTTTAGT	AATGTTTCAT	TTATCATCCA	780
G L T	K S V G	D K T	V F S	N V S F	I I H	
TAGTTTAGAC	CGTATTGGGA	TTATTGGTGT	CAATGGAACT	GGAAAGACAA	CACTATTAGA	840
S L D	R I G I	I G V	N G T	G K T T	L L D	
TGTTATTCG	GGTGAATTAG	GTTTGATGG	TGATCGTTCC	CCTTTTCAT	CAGCTAATGA	900
V I S	G E L G	F D G	D R S	P F S S	A N D	
TTATAAGATT	GCTTATTAAC	AACAAGAAC	AGACTTTGAT	GATTCTCAGA	CAATTTGGA	960
Y K I	A Y L K	Q E P	D F D	D S Q T	I L D	
CACCGTACTT	TCTTCTGACT	TAAGAGAGAT	GGCTTTAATT	AAAGAATATG	AATTATTGCT	1020
T V L	S S D L	R E M	A L I	K E Y E	L L L	
TAATCACTAC	GAAGAAAGTA	AGCAATCACG	TCTAGAGAAA	GTAATGGCAG	AAATGGATT	1080
N H Y	E E S K	Q S R	L E K	V M A E	M D S	
TTTAGATGCT	TGGTCTATTG	AGAGCGAAGT	CAAAACAGTA	TTATCCAAAT	TAGGTATTAC	1140
L D A	W S I E	S E V	K T V	L S K L	G I T	
TGATTTGCAG	TTGTCGGTTG	GTGAATTATC	AGGAGGATTA	CGAAGACGTG	TTCAATTAGC	1200
D L Q	L S V G	E L S	G G L	R R R V	Q L A	

GCAAGTATTA	TTAAATGATG	CAGATTATT	GCTCTTAGAC	GAACCTACTA	ACCACTTAGA	1260
Q V L	L N D A	D L L	L L D	E P T N	H L D	
TATTGACACT	ATTGCATGGT	TAACGAATT	TTTGAAAAAT	AGTAAAAGA	CAGTGCTTT	1320
I D T	I A W L	T N F	L K N	S K K T	V L F	
TATAACTCAT	GATCGTTATT	TTCTAGACAA	TGTTGCAACA	CGTATTTTG	AATTAGATAA	1380
I T H	D R Y F	L D N	V A T	R I F E	L D K	
GGCACAGATT	ACAGAATATC	AAGGCAATTA	TCAGGATTAT	GTCCGACTTC	GTGCAGAAC	1440
A Q I	T E Y Q	G N Y	Q D Y	V R L R	A E Q	
AGACGAGCGT	GATGCTGCTA	GTTTACATAA	AAAGAAACAG	CTTTATAAAC	AGGAACTAGC	1500
D E R	D A A S	L H K	K K Q	L Y K Q	E L A	
TTGGATGCGT	ACTCAGCCAC	AAGCTCGTGC	AACGAAACAA	CAGGCTCGTA	TTAATCGTT	1560
W M R	T Q P Q	A R A	T K Q	Q A R I	N R F	
TCAAAATCTA	AAAAACGATT	TACACCAAAC	AAGCGATACA	AGCGATTG	AAATGACATT	1620
Q N L	K N D L	H Q T	S D T	S D L E	M T F	
TGAAACAAAGT	CGAATTGGGA	AAAAGGTTAT	TAATTTGAA	AATGTCTCTT	TTTCTTACCC	1680
E T S	R I G K	K V I	N F E	N V S F	S Y P	
AGATAAAATCT	ATCTTGAAAG	ACTTTAATT	GTAAATTCAA	AATAAAGACC	GTATTGGCAT	1740
D K S	I L K D	F N L	L I Q	N K D R	I G I	
CGTTGGAGAT	AATGGTGTG	GAAAGTCAAC	CTTACTTAAT	TTAATTGTT	AAGATTTACA	1800
V G D	N G V G	K S T	L L N	L I V Q	D L Q	
GCCGGATTG	GGTAATGTCT	CTATTGGTGA	AACGATACGT	GTAGGTTACT	TTTCACAACA	1860
P D S	G N V S	I G E	T I R	V G Y F	S Q Q	
ACTTCATAAT	ATGGATGGCT	CAAAACGTGT	TATTAATTAT	TTGCAAGAGG	TTGCAGATGA	1920
L H N	M D G S	K R V	I N Y	L Q E V	A D E	
GGTTAAAAC	AGTGTGGTA	CAACAAGTGT	GACAGAACTA	TTGGAACAAT	TTCTCTTCC	1980
V K T	S V G T	T S V	T E L	L E Q F	L F P	
ACGTTCGACA	CATGGAACAC	AAATGCAAA	ATTATCAGGT	GGTGAGAAAA	AAAGACTTTA	2040
R S T	H G T Q	I A K	L S G	G E K K	R L Y	
CCTTTAAAAA	ATCCTGATTG	AAAAGCCTAA	TGTGTTACTA	CTTGATGAGC	CGACAAATGA	2100
L L K	I L I E	K P N	V L L	L D E P	T N D	
CTTAGATATT	GCTACATTAA	CTGTTCTGA	AAATTTTTA	CAAGGCTTG	GTGGTCCTGT	2160
L D I	A T L T	V L E	N F L	Q G F G	G P V	
GATTACAGTT	AGTCACGATC	GTTACTTTT	AGATAAAGTG	GCTAATAAAA	TTATTGCGTT	2220
I T V	S H D R	Y F L	D K V	A N K I	I A F	
TGAAGATAAC	GATATCCGTG	AATTTTTGG	TAATTATACT	GATTATTTAG	ATGAAAAGC	2280
E D N	D I R E	F F G	N Y T	D Y L D	E K A	
ATTTAATGAG	CAAAATAATG	AAGTTATCAG	TAAGGAGAG	AGTACCAAGA	CAAGTCGTGA	2340
F N E	Q N N E	V I S	K K E	S T K T	S R E	
AAAGCAAAGT	CGTAAAAGAA	TGTCTTACTT	TGAAAACAA	GAATGGGCGA	CAATTGAAGA	2400
K Q S	R K R M	S Y F	E K Q	E W A T	I E D	
CGATATTATG	ATATTGGAAA	ATACTATCAC	TCGTATAGAA	AATGATATGC	AAACATGTGG	2460

D I M I L E N T I T R I E N D M Q T C G	
TAGTGATTT ACAAGGTTAT CTGATTTACA AAAGGAATTA GATGCAAAAA ATGAAGCACT	2520
S D F T R L S D L Q K E L D A K N E A L	
TCTAGAAAAAG TATGACCGTT ATGAGTACCT TAGTGAGTTA GACACATGAT TATCCGTCG	2580
L E K Y D R Y E Y L S E L D T M I I R P	
ATTATTAAAAA ATGATGACCA AGCAGTTGCA CAATTAATTC GACAAAGTTT ACGCGCTAT	2640
I I K N D D Q A V A Q L I R Q S L R A Y	
GATTTAGATA AACCTGATAC AGCATATTCA GACCCTCACT TAGATCATTT GACCTCATAC	2700
D L D K P D T A Y S D P H L D H L T S Y	
TACGAAAAAA TAGAGAAGTC AGGATTCTTT GTCATTGAGG AGAGAGATGA GATTATTGGC	2760
Y E K I E K S G F F V I E E R D E I I G	
TGTGGCGGCT TTGGTCCGCT GAAAAATCTA ATTGCAGAGA TGCAAGAGT GTACATTGCA	2820
C G G F G P L K N L I A E M Q K V Y I A	
GAACGTTTCC GTGGTAAGGG GCTTGCTACT GATTTAGTGA AAATGATTGA AGTAGAAGCT	2880
E R F R G K G L A T D L V K M I E V E A	
CGAAAAATTG GGTATAGACA ACTTTATTTA GAGACAGCCA GTACTTTGAG TAGGGCAACT	2940
R K I G Y R Q L Y L E T A S T L S R A T	
GCGGTTTATA AGCATATGGG ATATTGTGCC TTATCGAAC CAATAGCAA TGATCAAGGT	3000
A V Y K H M G Y C A L S Q P I A N D Q G	
CATACAGCTA TGGATATTG GATGATTAAA GATTTATAAG TTGAAAGTGG ATTAGTGAAC	3060
H T A M D I W M I K D L	
ATGGATTAAT TATTTGAGA TAAGAGGAAA GAAAAGGAGA CATATATGGC ATATATTGG	3120
M A Y I W	
TCTTATTTGA AAAGGTACCC CAATGGTTA TGGCTTGATT TACTAGGAGC TATGCTTTT	3180
S Y L K R Y P N W L W L D L L G A M L F	
GTGACGGTTA TCCTAGGAAT GCCCACAGCC TTAGCGGGTA TGATTGATAA TGGCGTTACA	3240
V T V I L G M P T A L A G M I D N G V T	
AAAGGTGATC GGACTGGAGT TTATCTGTGG ACGTTCATCA TGTTTATATT TGTTGTACTA	3300
K G D R T G V Y L W T F I M F I F V V L	
GGTATTATTG GGC GTATTAC GATGGCTTAC GCATCTAGTC GCTTAACGAC AACAAATGATT	3360
G I I G R I T M A Y A S S R L T T T M I	
AGAGATATGC GTAATGATAT GTATGCTAAG CTTCAAGAAT ACTCCCATCA TGAATATGAA	3420
R D M R N D M Y A K L Q E Y S H H E Y E	
CAGATAGGTG TATCTTCACT AGTGACACGT ATGACAAGCG ATACTTTGT TTTGATGCAA	3480
Q I G V S S L V T R M T S D T F V L M Q	
TTTGCCTGAAA TGTCTTTACG TTTAGGCCTA GTAACTCCTA TGTTAATGAT TTTTGCCTG	3540
F A E M S L R L G L V T P M V M I F S V	
GTTATGATAC TAATTACGAG TCCATCTTGT GCTTGGCTTG TAGCGGTTGC GATGCCTCTT	3600
V M I L I T S P S L A W L V A V A M P L	
TTGGTAGGAG TCGTTTTATA TGTAGCTATA AAAACAAAAC CTTTATCTGA AAGACAACAG	3660
L V G V V L Y V A I K T K P L S E R Q Q	

ACTATGCTTG	ATAAAATCAA	TCAATATGTT	CGTGAAAATT	TAACAGGGTT	ACGCCTTGTT	3720													
T	M	L	D	K	I	N	Q	Y	V	R	E	N	L	T	G	L	R	V	V
AGAGCCTTTG	CAAGAGAGAA	TTTCAATCA	CAAAAATTTC	AAGTCGCTAA	CCAACGTTAC	3780													
R	A	F	A	R	E	N	F	Q	S	Q	K	F	Q	V	A	N	Q	R	Y
ACAGATACTT	CAACTGGTCT	TTTTAAATTA	ACAGGGCTAA	CAGAACCACT	TTTCGTTCAA	3840													
T	D	T	S	T	G	L	F	K	L	T	G	L	T	E	P	L	F	V	Q
ATTATTATTG	CAATGATTGT	GGCTATCGTT	TGGTTTGCTT	TGGATCCCTT	ACAAAGAGGT	3900													
I	I	I	A	M	I	V	A	I	V	W	F	A	L	D	P	L	Q	R	G
GCTATTAAAA	TAGGGGATTT	AGTTGCTTTT	ATCGAATATA	GCTTCATGC	TCTCTTTCA	3960													
A	I	K	I	G	D	L	V	A	F	I	E	Y	S	F	H	A	L	F	S
TTTTGCTAT	TTGCCAATCT	TTTACTATG	TATCCTCGTA	TGGTGGTATC	AAGCCATCGT	4020													
F	L	L	F	A	N	L	F	T	M	Y	P	R	M	V	V	S	S	H	R
ATTAGAGAGG	TGATGGATAT	GCCAACTCTCT	ATCAATCCTA	ATGCCGAAGG	TGTTACGGAT	4080													
I	R	E	V	M	D	M	P	I	S	I	N	P	N	A	E	G	V	T	D
ACGAAACTTA	AAGGGCATT	AGAATTGAT	AATGTAACAT	TCGTTATCC	AGGAGAAACA	4140													
T	K	L	K	G	H	L	E	F	D	N	V	T	F	A	Y	P	G	E	T
GAGAGTCCCG	TTTGTCATGA	TATTCTTTT	AAAGCTAAC	CTGGAGAAC	AATTGCTTT	4200													
E	S	P	V	L	H	D	I	S	F	K	A	K	P	G	E	T	I	A	F
ATTGGTCAA	CAGGTTCAAG	AAAATCTTCT	CTTGTAAATT	TGATTCCACG	TTTTTATGAT	4260													
I	G	S	T	G	S	G	K	S	S	L	V	N	L	I	P	R	F	Y	D
GTGACACTTG	GAAAAATCTT	AGTAGATGGA	GTTGATGTA	GAGATTATAA	CCTTAAATCA	4320													
V	T	L	G	K	I	L	V	D	G	V	D	V	R	D	Y	N	L	K	S
CTTCGCCAAA	AGATTGGATT	TATCCCCAA	AAAGCTCTT	TATTTACAGG	GACAATAGGA	4380													
L	R	Q	K	I	G	F	I	P	Q	K	A	L	L	F	T	G	T	I	G
GAGAATTAA	AATATGGAAA	AGCTGATGCT	ACTATTGATG	ATCTTAGACA	AGCGGTTGAT	4440													
E	N	L	K	Y	G	K	A	D	A	T	I	D	D	L	R	Q	A	V	D
ATTTCTCAAG	CTAAAGAGTT	TATTGAGAGT	CACCAAGAAG	CCTTGAAAC	GCATTTAGCT	4500													
I	S	Q	A	K	E	F	I	E	S	H	Q	E	A	F	E	T	H	L	A
GAAGGTGGGA	GCAATCTTC	TGGGGGTCAA	AAACAAACGGT	TATCTATTGC	TAGGGCTGTT	4560													
E	G	G	S	N	L	S	G	G	Q	K	Q	R	L	S	I	A	R	A	V
GTAAAGATC	CAGATTTATA	TATTTTGAT	GATTCATTT	CTGCTCTCGA	TTATAAGACA	4620													
V	K	D	P	D	L	Y	I	F	D	D	S	F	S	A	L	D	Y	K	T
GACGCTACTT	TAAGAGCGCG	TCTAAAAGAA	GTAACCGGTG	ATTCTACAGT	TTTGATAGTT	4680													
D	A	T	L	R	A	R	L	K	E	V	T	G	D	S	T	V	L	I	V
GCTCAAAGGG	TGGGTACGAT	TATGGATGCT	GATCAGATTA	TTGTCCTTGA	TGAAGGCGAA	4740													
A	Q	R	V	G	T	I	M	D	A	D	Q	I	I	V	L	D	E	G	E
ATTGTCGGTC	GTGGTACCCA	CGCTCAATT	ATAGAAAATA	ATGCTATT	TCGTGAAATC	4800													
I	V	G	R	G	T	H	A	Q	L	I	E	N	N	A	I	Y	R	E	I
GCTGAGTCAC	AACTGAAGAA	CCAAAACCTA	TCAGAAGGAG	AGTGATTGTA	TGAGAAAAAA	4860													
A	E	S	Q	L	K	N	Q	N	L	S	E	G	E	M	R	K	K		

|---->

ATCTGTTTTT TTGAGATTAT GGTCTTACCT AACTCGCTAC AAAGCTACTC TTTTCTTAGC	4920
S V F L R L W S Y L T R Y K A T L F L A	
GATTTTTTTG AAAGTTTAT CTAGTTTAT GAGTGTCTG GAGCCTTTA TTTTAGGGTT	4980
I F L K V L S S F M S V L E P F I L G L	
AGCGATAACA GAGTTGACTG CTAACCTTGT TGATATGGCT AAGGGAGTTT CTGGGGCAGA	5040
A I T E L T A N L V D M A K G V S G A E	
ATTGAACGTT CCTTATATTG CTGGTATTTT GATTATTAT TTTTCAGAG GTGTTTCTA	5100
L N V P Y I A G I L I I Y F F R G V F Y	
TGAATTAGGT TCTTATGGCT CAAATT (SEQ ID NO:7)	5126
E L G S Y G S N	

FIG. 2a

NFDIETTTFE AMKKHASLLE KISVERSFIE FDKLLLAPYW RKGMLALIDS	50
HAFNYLPCLK NRELQLSAFL SQLDKDFLFE TSEQAWASLI LSMEVEHTKT	100
FLKKWKTSTH FQKDVEHIVD VYRIREQMGL AKEHLYRYGK TIIKQAEGIR	150
KARGLMVDFE KIEQLDSELA IHDRHEIVVN GGTLIKKLGI KPGPQMGDII	200
SQIELAIVLG QLINEEEAIL HFVKQYLM (SEQ ID NO:8)	229

FIG. 2b

MSDFLVDGLT KSVGDKTVFS NVSFIIHSLD RIGIIGVNGT GKTTLLDVIS	50
GELGFDGDRS PFSSANDYKI AYLKQEPDFD DSQTILDVTI SSDLREMALI	100
KEYELLLNHY EESKQSRLEK VMAEMDSLDA WSIESEVKTV LSCLGITDLQ	150
LSVGELSGGL RRRVQLAQVL LNDADLLLLD EPTNHLDIDT IAWLTNFLKN	200
SKKTVLFITH DRYFLDNVAT RIFELDKAQI TEYQGNYQDY VRLRAEQDER	250
DAASLHKKKQ LYKQELAWMR TQPQARATKQ QARINRFQNL KNDLHQTSDT	300
SDLEMTFETS RIGKKVINFE NVSFSPDKS ILKDFNLLIQ NKDRIGIVGD	350
NGVGKSTLLN LIVQDLQPDS GNVSIGETIR VGYFSQQLHN MDGSKRVINY	400
LQEVADEVKT SVGTTSVTEL LEQFLFPRST HGTQIAKLSG GEKKRLYLLK	450
ILIEKPNVLL LDEPTNDLDI ATLTVLENFL QGFGGPVITV SHDRYFLDKV	500
ANKIIAFEDN DIREFFGNYT DYLDEKAFNE QNNEVISKKE STKTSREKQS	550
RKRMSYFEKQ EWATIEDDIM ILENTITRIE NDMQTCGSDF TRLSDLQKEL	600
DAKNEALLEK YDRYEYLSEL DT (SEQ ID NO:9)	622

FIG. 2c

MIIRPIIKND DQAVAQLIRQ SLRAYDLDKP DTAYSDPHLD HLTSYYEKIE	50
KSGFFVIEER DEIIGCGGFG PLKNLIAEMQ KVYIAERFRG KGLATDLVKM	100
IEVEARKIGY RQLYLETAST LSRATAVYKH MGYCALSQPI ANDQGHTAMD	150
IWMIKDL (SEQ ID NO:10)	157

FIG. 2d

MAYIWSYLRK	YPNWLWLDLL	GAMLFVTVIL	GMPTALAGMI	DNGVTKGDRT	50
GVYLWTFIMF	IFVVLGIIGR	ITMAYASSRL	TTTMIRDMRN	DMYAKLQEYS	100
HHEYEQIGVS	SLVTRMTSDT	FVLMQFAEMS	LRLGLVTPMV	MIFSVVMILI	150
TSPSLAWLVA	VAMPLLVGVV	LYVAIKTKPL	SERQQTMLDK	INQYVRENLT	200
GLRVVRAFAR	ENFQSQKFQV	ANQRYTDTST	GLFKLTGLTE	PLFVQIIIAM	250
IVAIIVWFALD	PLQRGAIKIG	DLVAFIEYSF	HALFSFLLFA	NLFTMYPRMV	300
VSSHRIREVM	DMPISINPNA	EGVTDTKLKG	HLEFDNVTFA	YPGETESPVL	350
HDISFKAKPG	ETIAFIGSTG	SGKSSLVNLI	PRFYDVTLGK	ILVDGVDVRD	400
YNLKSLRQKI	GFIPQKALLF	TGTIGENLKY	GKADATIDDL	RQAVDISQAK	450
EFIESHQEAF	ETHLAEGGSN	LSGGQKQRLS	IARAVVKDPD	LYIFDDSFSA	500
LDYKTDATLR	ARLKEVTGDS	TVLIVAQRVG	TIMDADQIIV	LDEGEIVGRG	550
THAQLIENNA	IYREIAESQL	KNQNLSEGE	(SEQ ID NO:11)		579

FIG. 2e

MRKKSVFLRL	WSYLTRYKAT	LFLAIFLKVL	SSFMSVLEPF	ILGLAITELT	50
ANLVDMAKGV	SGAELNVPYI	AGILIIYFFR	GVFYELGSYG	SN	92
(SEQ ID NO:12)					

FIG. 2f

AATTTGGAAG TGCTCTATCA ACAGTTGAAG TAAAGGAGAT TATTAGTGAA GAAAACATAT 60
 F G S A L S T V E V K E I I S E E N I W
 ---->
 GGTTATATCG GCTCAGTTGC TGCCATTTA CTAGCTACTC ATATTGGAAG TTACCAACTT 120
 L Y R L S C C H F T S Y S Y W K L P T W
 GGTAAGCATC ATATGGGTCT AGCAACAAAG GACAATCAGA TTGCCTATAT TGATGACAGC 180
 M G L A T K D N Q I A Y I D D S
 |---->
 AAAGGTAAGG CAAAAGCCCC TAAAACAAAC AAAACGATGG ATCAAATCAG TGCTGAAGAA 240
 K G K A K A P K T N K T M D Q I S A E E
 GGCATCTCTG CTGAACAGAT CGTAGTCAAA ATTACTGACC AAGGCTATGT GACCTCACAC 300
 G I S A E Q I V V K I T D Q G Y V T S H
 GGTGACCATT ATCATTTTA CAATGGAAA GTTCCTTATG ATGCGATTAT TAGTGAAGAG 360
 G D H Y H F Y N G K V P Y D A I I S E E
 TTGTTGATGA CGGATCCTAA TTACCGTTT AAACAATCAG ACGTTATCAA TGAAATCTTA 420
 L L M T D P N Y R F K Q S D V I N E I L
 |---->
 GACGGTTACG TTATTAAAGT CAATGGCAAC TATTATGTTT ACCTCAAGCC AGGTAGTAAG 480
 D G Y V I K V N G N Y Y V Y L K P G S K
 CGCAAAACAA TTCGAACCAA ACAACAAATT GCTGAGCAAG TAGCCAAAGG AACTAAAGAA 540
 R K N I R T K Q Q I A E Q V A K G T K E
 GCTAAAGAAA AAGGTTTAGC TCAAGTGGCC CATCTCAGTA AAGAAGAAGT TGCGGCAGTC 600
 A K E K G L A Q V A H L S K E E V A A V
 AATGAAGCAA AAAGACAAGG ACGCTATACT ACAGACGATG GCTATATTT TAGTCCGACA 660
 N E A K R Q G R Y T T D D G Y I F S P T
 GATATCATTG ATGATTTAGG AGATGCTTAT TTAGTACCTC ATGTTAATCA CTATCATTAT 720
 D I I D D L G D A Y L V P H G N H Y H Y
 ATTCCCTAAAA AGGATTTGTC TCCAAGTGAG CTAGCTGCTG CACAAGCCTA CTGGAGTC 780
 I P K K D L S P S E L A A A Q A Y W S Q
 AAACAAAGGTC GAGGTGCTAG ACCGCTGTAT TACCGCCCGA CACCAAGCCCC AGGTCGTAGG 840
 K Q G R G A R P S D Y R P T P A P G R R
 AAAGCCCCAA TTCCTGATGT GACGCCAAAC CCTGGACAAG GTCATCAGCC AGATAACGGT 900
 K A P I P D V T P N P G Q G H Q P D N G
 GGCTATCATC CAGCGCCTCC TAGGCCAAAT GATGCGTCAC AAAACAAACA CCAAAGAGAT 960
 G Y H P A P P R P N D A S Q N K H Q R D
 GAGTTTAAAG GAAAAACCTT TAAGGAACCTT TTAGATCAAC TACACCGTCT TGATTTGAAA 1020
 E F K G K T F K E L L D Q L H R L D L K
 TACCGTCATG TGGAAGAAGA TGGGTTGATT TTTGAACCGA CTCAAGTGAT CAAATCAAAC 1080
 Y R H V E E D G L I F E P T Q V I K S N
 GCTTTGGGT ATGTGGTGCCTC TCATGGAGAT CATTATCATA TTATCCCAAG AAGTCAGTTA 1140
 A F G Y V V P H G D H Y H I I P R S Q L
 TCACCTCTTG AAATGGAATT AGCAGATCGA TACTTAGCTG GCCAAACTGA GGACAATGAC 1200
 S P L E M E L A D R Y L A G Q T E D N D
 TCAGGTTCAAG AGCACTCAAAC ACCATCAGAT AAAGAAGTGA CACATACCTT TCTTGGTCAT 1260

S	G	S	E	H	S	K	P	S	D	K	E	V	T	H	T	F	L	G	H							
CGCATCAAAG	CTTACGGAAA	AGGCTTAGAT	GGTAAACCAT	ATGATACGAG	TGATGCTTAT	1320	R	I	K	A	Y	G	K	G	L	D	G	K	P	Y	D	T	S	D	A	Y
GTFFFFTAGTA	AAGAATCCAT	TCATTCACTG	GATAAAATCAG	GAGTTACAGC	TAAACACGGA	1380	V	F	S	K	E	S	I	H	S	V	D	K	S	G	V	T	A	K	H	G
GATCATTTC	ACTATATAGG	ATTTGGAGAA	CTTGAACAAT	ATGAGTTGGA	TGAGGTCGCT	1440	D	H	F	H	Y	I	G	F	G	E	L	E	Q	Y	E	L	D	E	V	A
AACTGGGTGA	AAGCAAAAGG	TCAAGCTGAT	GAGCTTGCTG	CTGCTTTGGA	TCAGGAACAA	1500	N	W	V	K	A	K	G	Q	A	D	E	L	A	A	A	L	D	Q	E	Q
GGCAAAGAAA	AACCACTCTT	TGACACTAAA	AAAGTGAGTC	GCAAAGTAAC	AAAAGATGGT	1560	G	K	E	K	P	L	F	D	T	K	K	V	S	R	K	V	T	K	D	G
AAAGTGGGCT	ATATGATGCC	AAAAGATGGT	AAGGACTATT	TCTATGCTCG	TGATCAACTT	1620	K	V	G	Y	M	M	P	K	D	G	K	D	Y	F	Y	A	R	D	Q	L
GATTGACTC	AGATTGCCTT	TGCCGAACAA	GAACATAATGC	TTAAAGATAAA	GAAGCATTAC	1680	D	L	T	Q	I	A	F	A	E	Q	E	L	M	L	K	D	K	K	H	Y
CGTTATGACA	TTGTTGACAC	AGGTATTGAG	CCACGACTTG	CTGTAGATGT	GTCAAGTCTG	1740	R	Y	D	I	V	D	T	G	I	E	P	R	L	A	V	D	V	S	S	L
CCGATGCATG	CTGGTAATGC	TACTTACGAT	ACTGGAAGTT	CGTTTGTAT	CCCACATATT	1800	P	M	H	A	G	N	A	T	Y	D	T	G	S	S	F	V	I	P	H	I
GATCATATCC	ATGTCGTTCC	GTATTCATGG	TTGACGCGCG	ATCAGATTGC	AACAGTCAAG	1860	D	H	I	H	V	V	P	Y	S	W	L	T	R	D	Q	I	A	T	V	K
TATGTGATGC	AACACCCCGA	AGTCGTCGG	GATGTATGGT	CTAAGCCAGG	GCATGAAGAG	1920	Y	V	M	Q	H	P	E	V	R	P	D	V	W	S	K	P	G	H	E	E
TCAGGTTCGG	TCATTCCAAA	TGTTACGCCT	CTTGATAAAC	GTGCTGGTAT	GCCAAACTGG	1980	S	G	S	V	I	P	N	V	T	P	L	D	K	R	A	G	M	P	N	W
CAAATTATCC	ATTCTGCTGA	AGAAGTTCAA	AAAGCCCTAG	CAGAAGGTCG	TTTTGCAACA	2040	Q	I	I	H	S	A	E	E	V	Q	K	A	L	A	E	G	R	F	A	T
CCAGACGGCT	ATATTTTCGA	TCCACGAGAT	GTGTTGGCCA	AAGAAACTTT	TGTATGGAAA	2100	P	D	G	Y	I	F	D	P	R	D	V	L	A	K	E	T	F	V	W	K
GATGGCTCCT	TTAGCATCCC	AAGAGCAGAT	GGCAGTCAT	TGAGAACCAT	TAATAAATCT	2160	D	G	S	F	S	I	P	R	A	D	G	S	S	L	R	T	I	N	K	S
GATCTATCCC	AAGCTGAGTG	GCAACAAGCT	CAAGAGTTAT	TGGCAAAGAA	AAATACTGGT	2220	D	L	S	Q	A	E	W	Q	Q	A	Q	E	L	L	A	K	K	N	T	G
GATGCTACTG	ATACGGATAA	ACCCAAAGAA	AAGCAACAGG	CAGATAAGAG	CAATGAAAAC	2280	D	A	T	D	T	D	K	P	K	E	K	Q	Q	A	D	K	S	N	E	N
CAACAGCCAA	GTGAAGCCAG	TAAAGAAGAA	AAAGAACATCAG	ATGACTTTAT	AGACAGTTA	2340	Q	Q	P	S	E	A	S	K	E	E	K	E	S	D	D	F	I	D	S	L
CCAGACTATG	GTCTAGATAG	AGCAACCTA	GAAGATCATA	TCAATCAATT	AGCACAAAAAA	2400	P	D	Y	G	L	D	R	A	T	L	E	D	H	I	N	Q	L	A	Q	K
GCTAATATCG	ATCCTAAGTA	TCTCATTTTC	CAACCAGAAG	GTGTCCAATT	TTATAATAAA	2460	A	N	I	D	P	K	Y	L	I	F	Q	P	E	G	V	Q	F	Y	N	K

AATGGTGAAT TGGTAACCTA TGATATCAAG ACACCTCAAC AAATAAACCC TTAACCAAAA 2520
 N G E L V T Y D I K T L Q Q I N P
 GAAGATCTCA TTGTTAAAGC ACTGCTTGAT CAAAGCAAGT TACGGTGATT TTGAAGTCAT 2580
 TCTATGTAAC GAGTAGTGAT AAAAGTTGGA TAATAGCGGT TTTCTTTGC AAAGAAATGG 2640
 TATCCATGTT AGAATAGTAA AAAAAGAGGA GGATTCTTGG ACTAATGTCA AATAAGTAGA 2700
 CAGAAAACGT TGTTATTTA TTGCGTTAAA ATAATTTCT TCTTCTGAT TAGGGTTAG 2760
 .K I A N F Y N E E K Q N P T L
 TCCTAGATTA GCCGTATGTG GGTTGTAATT GTTATAAAAA TTCTCAATGT ATTCAAAGCA 2820
 G L N A T H P N Y N N Y F N E I Y E F C
 GTCTAATTGA ACCTGTTGA TATTTGATA ATGTTTCGG TTGATTTGTC TATGCTTAA 2880
 D L Q V Q K I N Q Y H K R N I Q R H K L
 ATACTTGAAA AATGCTTCAG TTACGGCATT ATCATAAGGA TATCCAGGAT TAGAAAAAGA 2940
 Y K F F A E T V A N D Y P Y G P N S F S
 ATGCATGATA TTGGCACTGC ACCCTAATAG TGAGACGCAA GAAAAACACT TTTAGGCAAT 3000
 H M
 <----|
 CAGTTTCTG TACTGTACAG GCGACTGGTC GTTTAATCTC TGTTGAATTG TAGTTTCATT 3060
 L K R Y Q V P S Q D N L R Q Q I R T E N
 ATAAAATGTA ATGTAATTT TAACAATATT TGTTATACTA TCTTGTGTTG ATTTTCCTCCT 3120
 Y F T I Y N K V I N T I S D K N Y K R R
 ATTATGGAAA TAAAAGGTTT CAGTCTTAG GACGGTGTGA AACCATTCAA TACAGGCATT 3180
 N H F Y F T E T K L V T H F W E I C A N
 ATCTGCAGGT GTTCCTTTC GAGACATTGA GCGGATAATG TCTTTTCCG TGCAAGCCTG 3240
 D A P T G K R S M S R I I D K E T C A Q
 GTAGTAAGCC ATAGAAGTAT ACACTGAGCC TTGGTCACTG TGTAAGATTG CTCTTTATT 3300
 Y Y A M
 <----|
 TAGGCAATTT TAACTGATTA AGGGTGTCTA GTACAAAATC CGTGTCTGA CAATCTGAGA 3360
 K P L K L Q N L T D L V F D T D Q C D S
 TAGTGTAAGC TATAATTCT CGGTTATAGA GATTCTAAAT TGATGAGAGA TACAATTAC 3420
 I T Y A I I E R N Y L N M I S S L Y L K
 AGTTACCGAA ATATAGGTAG GTAATATCTG TTACGAGCTT TTCTTAGGC TTATCGGCAT 3480
 C N G F Y L Y T I D T V L K E K P K D A
 GGAAATCCCG ACTCAATTAA TTATCTGTTA AATAATAAGC TTTACCCAAA TTGGGAACCTT 3540
 H G D R S L K N D T L Y Y A K G L N P V
 TCTGGTACG TGTCCGACAA AGCCAGCCAT TATTTTCAT GATACGATAG ACTTTCTTTG 3600
 K K T R T R C L W G N N K M I R Y V K K
 TATTAACAGT CAATCCGTGG ATTTTTTGAT GCAATCGTGT AATGGTACGA TAGCCATAAA 3660
 T N V T L G H I K K L L R T I T R Y G Y
 TAAAGTGATT CTCCATACAG AGCTGTTCAA TTAATTCAAT AAGGTCAATCT TTTTTGCGG 3720
 I F H N E M
 <----|

CTTCTCATAAC	TCCTTTTCC	AACGGTAATA	GGTCGACCGC	TTGACCTAA	AACAGTCTAG	3780
AATGAAAAC	ATCGGGTAGT	TGTTTTATA	GTCTCCACA	AGCTTGATAA	GACTTACTTT	3840
ATCGATTTCC	TTATCAAGCC	TCGACTACTT	TTTAAGAGGT	CAACCTGTAA	TTGTAATTGT	3900
I S K R I L G	R Y K K L L	D V Q L	Q L Q			
TCCACTTCAG	ACAGATGTTC	CAAGCCTTA	CCGTAGGTAT	ATTGCTTGCC	AACACCTTGA	3960
E V E S L H E	L G K G Y T	Y Q K G	V G Q			
TGAAAACGAT	AAAGCTCC	GTTTCGTAC	CATTCATCC	AAGTATAGAT	TTGACTATT	4020
H F R Y L E E	N E Y W K M	W T Y I	Q S N			
TTTTGATGC	CTAAAGTCTC	CATAATACT	CTGTTAGACT	TGCCTGCTT	CTTCATATCG	4080
N K I G L T E	M I V R N S	K G A K	K M D			
ATGCAAGCCA	GCTTAGTTTC	CCATGAATAT	GCTTTTTAA	CCATAATAAA	ACATTCTGT	4140
I C A L K T E	W S Y A K K	V M				
<----						
TTCTAGTTA	CTAAATTCA	ACAGGAGTGT	TTTCTTTG	TCTCATTAA	GGGATTCA	4200
GCCTATTGTT	GTCATCAATT	ATTTTCTAA	ATTCCCCGGA	CTTAAATTGT	GACCCTGGT	4260
CGGAATGAAA	GAGAAGTGT	CCTCAATCT	TTCTTTATT	AAGTAAAAG	GCAACACTT	4320
TCTGTACAAC	ATTTATAAAAG	TGTTTTCTA	GGCAATTAAT	CTTTAGTCA	TTGGTGT	4380
				A I L R K T	M P T Q	
GTAGTTGAGA	CTACCATGAA	TGCGGTGGTA	ATTCCACCAA	TGAACATAGT	CTTTAGTCTT	4440
Y N L S G H	I R H Y	N W W H	V Y	D K T K		
AAGAGCTAGT	TCTTCCAGCA	ATTGAAAGGT	TTCTTGATAA	ACAAATTCAA	TTTGAAAGC	4500
L A L E E L	L Q F T	E Q Y V F	E I K F A			
ACGATACGTA	CTTCAGCTA	CGGCATTGTC	ATAAGGATAA	CCAGCCTGAC	TAAGCGAACG	4560
R Y T S E A	V A N D	Y P Y G A Q	S L S R			
TGTGATTCCA	AAGGCTTCCA	ATATTCATC	AATTAACTGA	TTATCAAAC	CTTGCCACG	4620
T I G F A E	L I E D	I L Q N D F	E K G R			
ATCTGAATGG	AACATCTTGA	CTTGGTCAG	GGCGTAAGGG	ATGCTTGTA	TGGCTTGCTT	4680
D S H F M K	V K T L	A Y P I S Q	I A Q K			
AACGAGTTCA	GCGGTCTTGT	GCCAACCAAG	AGACAGGCCG	ATGATTCAC	GGTTGTATAG	4740
V L E A T K	H W G L	S L G I I E	R N Y L			
GTCAATGATG	AGGCAAACAT	AAGCCAACG	ATTGCCTACA	CGAACATAGG	TTAAGTCAGT	4800
D I I L C V	Y A W R	N G V R V Y	T L D T			
GACTAAGGCT	TGTAGTGGTC	TTCTTGCTT	AAATTGCC	TCTAAGTGGT	TGGGAATAGG	4860
V L A Q L P	R E Q K	F Q R D L H	N P I P			
GGCTTCATTC	TTGCCTCTAG	AATGTGGTT	GAAGGGGCT	TTCTGATAAA	CAGAAACCAA	4920
A E N K G R	S H P K	F T A K Q Y	V S V L			
ATTGAGTCGC	TTCATAATGC	GTCGAATCCG	ACGACGTGAA	AGTGTGATAC	CTTCGTTATT	4980
N L R K M I	R R I R	R R S L T I	G E N N			
CAAGCATATT	TTGATTTTC	TGGATCCGTA	TCTAGACTCG	CTATCGAGAA	AAATTCTTT	5040
L C I K I K	R S G Y	R S E S D L	F I R K			

AATAGTTTCT TCAAACCTCCG TTTCAGATAC TGACTCCACG GCTTGATAGT AATAACTTGA 5100
 I T E E F E T E S V S E V A Q Y Y Y S S
 GTGTGGCATA TTCAGCCAGC GACACATCTT TGAAATGCTG TATTTATCCT TATTAGCAGT 5160
 H P M N L W R C M K S I S Y K D K N A T
 GATTATTC CTTTTGTGC CATAATCACC GCTGCTTGCT TTAGGATATC TAATT 5215
 I I E R K T G Y D G S S A K P Y R I
 (SEQ ID NO:13) <----|

FIG. 3a

FGSALSTVEV KEIISEENIW LYRLSCCHFT SYSYWKLPTW 40
 (SEQ ID NO:14)

FIG. 3b

MGLATKDNQI AYIDDSKGKA KAPKTNKTMD QISAEEGISA EQIVVKITDQ 50
 GYVTSHGDHY HFYNGKVPYD AIISEELLMT DPNYRFKQSD VINEILDGYV 100
 IKVNGNYYVY LKPGSKRKNI RTKQQIAEQV AKGTKEAKEK GLAQVAHLSK 150
 EEVAAVNEAK RQGRYTTDDG YIFSPTDIID DLGDAYLVPH GNHYHYIPKK 200
 DLSPSELAAA QAYWSQKQGR GARPSDYRPT PAPGRRKAPI PDVTPNPGQG 250
 HQPDNGGYHP APPRPNDASQ NKHQRDEFKG KTFKELLDQL HRLDLKYRHV 300
 EEDGLIFEPT QVIKSNAFGY VVPHGDHYHI IPRSQLSPLE MELADRYLAG 350
 QTEDNDSGSE HSKPSDKEVT HTFLGHRIKA YGKGLDGKPY DTSDAYVFSK 400
 ESIHSVDKSG VTAKHGDHFH YIGFGELEQY ELDEVANWVK AKGQADELAA 450
 ALDQEQQKEK PLFDTKKVSR KVTKDGKVGY MMPKDGKDYF YARDQLDLTQ 500
 IIAFAEQELML KDKKHYRYDI VDTGIEPRLA VDVSSLPMHA GNATYDTGSS 550
 FVIPHIDHIH VVPYSWLTRD QIATVKYVMQ HPEVRPDVWS KPGHEESGSV 600
 IPNVTPLDKR AGMPNWQIIH SAEEVQKALA EGRFATPDGY IFDPRDVLA 650
 ETFVWKDGGSF SIPRADGSSL RTINKSDLSQ AEWQQAQELL AKKNTGDATA 700
 TDKPKEKQQA DKSNENQQPS EASKEEKESD DFIDSLPDYG LDRATLEDHI 750
 NQLAQKANID PKYLIFQPEG VQFYNNKNGEL VTYDIKTLQQ INP 793
 (SEQ ID NO:15)

FIG. 3c

MTDPNYRFKQ	SDVINEILDG	YVIKVNGNYY	VYLPGSKRK	NIRTKQQIAE	50
QVAKGTKEAK	EKGGLAQVAHL	SKEEVAAVNE	AKRQGRYTTD	DGYIFSPPTDI	100
IDDLGDAYLV	PHGNHYHYIP	KKDLSPSELA	AAQAYWSQKQ	GRGARPSDYL	150
PTPAPGRRKA	PIPDVTPNPG	QGHQPDNGGY	HPAPPRPNDA	SQNKHQRDEF	200
KGKTFKELLD	QLHRLDLKYR	HVEEDGLIFE	PTQVIKSNAF	GYVVPHGDHY	250
IIIPRSQLSP	LEMELEADRYL	AGQTEDNDSG	SEHSKPSDKE	VTHTFLGHRI	300
KAYGKGLDGK	PYDTSDAYVF	SKESIHSVDK	SGVTAKHGDH	FHYIGFGELE	350
QYELDEVANW	VKAKGQADEL	AAALDQEQQK	EKPLFDTKKV	SRKVTKDGKV	400
GYMMPKDGKD	YFYARDQLDL	TQIAFAEQEL	MLKDKKHYRY	DIVDTGIEPR	450
LAVDVSSLPM	HAGNATYDTG	SSFVIPHIDH	IHVVPYSWLT	RDQIATVKYV	500
MQHPEVRPDV	WSKPGHEESG	SVIPNVTPLD	KRAGMPNWQI	IHSAAEVQKA	550
LAEGRFATPD	GYIFDPRDVL	AKETFWKDG	SFSIPRADGS	SLRTINKSDL	600
SQAEWQQAQE	LLAKKNTGDA	TDTDKPKEKQ	QADKSNNENQQ	PSEASKEEKE	650
SDDFIDSLPD	YGLDRATLED	HINQLAQKAN	IDPKYLIFQP	EGVQFYNKNG	700
ELVTYDIKTL	QQINP	(SEQ ID NO:16)			715

FIG. 3d

MHSFSNPGYP	YDNAVTEAFF	KYLKHRQINR	KHYQNIKQVQ	LDCFEYIENF	50
YNNYNPHTAN	LGLTPNQKEE	NYFNAIK	(SEQ ID NO:17)		77

FIG. 3e

MAYYQACTEK	DIIRSMSRKKG	TPADNACIEW	FHTVLKTETF	YFHNRRKYNK	50
DSITNIVKNY	ITFYNETRIQ	QRLNDQSPVQ	YRKLIA	(SEQ ID NO:18)	86

FIG. 3f

MENHFIYGYR	TITRLLKKIH	GLTVNTKKVY	RIMKNNGWLC	RTRTKKVPNL	50
GKAYYLTDNK	LSRDFHADKP	KEKLVTDITY	LYFGNCKLYL	SSIMNLYNRE	100
IIAYTISDCQ	DTDFVLDTLN	QLKLPK	(SEQ ID NO:19)		126

FIG. 3g

MVKKAYSWET KLACIDMKKA GKSNRVIMET LGIKNNNSQIY TWMKWYENEE 50
 LYRFHQGVGK QTYYGKGLEH LSEVEQLQLQ VDLLKKYRGL IRKSIK 96
 (SEQ ID NO:20)

FIG. 3h

IRYPKASSGD YGKREIITA NKDKYSISKM CRWLNMPHSS YYYQAVESVS 50
 ETEFEETIKR IFLDSESRYG SRKIKICLNN EGITLSRRRI RRIMKRLNLV 100
 SVYQKATFKP HSRGKNEAPI PNHLDRQFKQ ERPLQALVTD LTYVRVGNRW 150
 AYVCLIIDLY NREIIGLSLG WHKTAELVKQ AIQSIPYALT KVKMFHSDRG 200
 KEFDNQLIDE ILEAFGITRS LSQAGYPYDN AVAESTYRAF KIEFVYQETF 250
 QLLEELALKT KDYVHWWNYH RIHGSINYQT PMTKRLIA (SEQ ID NO:21) 288

FIG. 3i

AATTGAAAG CAGAATTATC TGTAGAAGAT GAGCAATATA CAGCAACAGT TTATGGTAAA 60
 N L K A E L S V E D E Q Y T A T V Y G K
 ----->
 TCTGCTCATG GTTCAACACC ACAAGAAGGT GTTAATGGGG CGACTTATTT AGCTCTTAT 120
 S A H G S T P Q E G V N G A T Y L A L Y
 CTAAGTCAAT TTGATTTGA AGGTCTGCT CGTGCTTCT TAGATGTTAC AGCCAACATT 180
 L S Q F D F E G P A R A F L D V T A N I
 ATTCACGAAG ACTTCTCAGG TGAAAAACTT GGAGTAGCTT ATGAAGATGA CTGTATGGGA 240
 I H E D F S G E K L G V A Y E D D C M G
 CCATTGAGCA TGAATGCAGG TGTCTTCCAG TTTGATGAAA CTAATGATGA TAATACTATC 300
 P L S M N A G V F Q F D E T N D D N T I
 GCTCTTAATT TCCGTTACCC ACAAGGGACA GATGCTAAA CTATCCAAAC TAAGCTTGAG 360
 A L N F R Y P Q G T D A K T I Q T K L E
 AAACCTAACG GAGTTGAAAA AGTAGCTCTT TCTGACCATG AACACACACC AACTATGTA 420
 K L N G V E K V T L S D H E H T P H Y V
 CCTATGGACG ATGAATTAGT ATCAACCTTA CTAGCTGTCT ATGAAAAGCA AACTGGCTT 480
 P M D D E L V S T L L A V Y E K Q T G L
 AAAGGACATG AACAGGTTAT TGGTGGTGGG ACATTTGGTC GCTTACTTGA ACGGGGTGT 540
 K G H E Q V I G G G T F G R L L E R G V
 GCATACGGTG CCATGTTCCC AGGAGATGAA AACACTATGC ATCAAGCTAA TGAGTACATG 600
 A Y G A M F P G D E N T M H Q A N E Y M
 CCTTTAGAAA ATATTTCCG TTCGGCTGCT ATCTACGCAG AAGCTATCTA TGAATTAATC 660

P	L	E	N	I	F	R	S	A	A	I	Y	A	E	A	I	Y	E	L	I	
AAATAAAAATA ATCCTTAAAC TAAATATGTG ATCAATGATA AAGGGTGGTG AAGACATGAA																	720			
K .																				
AGTGTCTTG CCTCTTTCA TAAGGTTAGA TTTGGAGACT TTATGACTGA CTTGGAAAAA																	780			
M T D L E K ----->																				
ATTATTAAAG CAATAAAAAG TGATTACAG AATCAAAATT ATACAGAAAA TGGTATTGAT																	840			
I	I	K	A	I	K	S	D	S	Q	N	Q	N	Y	T	E	N	G	I	D	
CCTTGTTTG CTGCTCCTAA AACAGCTAGG ATCAATATTG TTGGCCAAGC ACCTGGTTA																	900			
P	L	F	A	A	P	K	T	A	R	I	N	I	V	G	Q	A	P	G	L	
AAAACCTCAAG AAGCAAGACT CTATTGGAAA GATAAATCTG GAGATCGTCT ACGCCAGTGG																	960			
K	T	Q	E	A	R	L	Y	W	K	D	K	S	G	D	R	L	R	Q	W	
CTTGGAGTTG ATGAAGAGAC ATTTTACCAT TCTGGAAAAT TTGCTGTTT ACCTTTAGAT																	1020			
L	G	V	D	E	E	T	F	Y	H	S	G	K	F	A	V	L	P	L	D	
TTTTATTACC CAGGCAAAGG AAAATCAGGA GATTTACCCC CTAGAAAAGG TTTGCGGAG																	1080			
F	Y	Y	P	G	K	G	K	S	G	D	L	P	P	R	K	G	F	A	E	
AAATGGCACC CTCTTATTT AAAAGAAATG CCTAATGTTA AATTGACCTT GCTAGTTGGT																	1140			
K	W	H	P	L	I	L	K	E	M	P	N	V	Q	L	T	L	L	V	G	
CAGTATGCTC AGAAATATTA TCTTGGAAAGC TCCGCACATA AAAATCTAAC AGAAACAGTT																	1200			
Q	Y	A	Q	K	Y	Y	L	G	S	S	A	H	K	N	L	T	E	T	V	
AAAGCTTACA AAGACTATCT ACCCGATTAT TTACCCCTGG TTCACCCATC ACCGCGAAAT																	1260			
K	A	Y	K	D	Y	L	P	D	Y	L	P	L	V	H	P	S	P	R	N	
CAAATTTGGC TAAAGAAGAA TCCATGGTTT GAAAAGATC TAATCGTTGA TTTACAAAAG																	1320			
Q	I	W	L	K	K	N	P	W	F	E	K	D	L	I	V	D	L	Q	K	
ATAGTAGCAG ATATTTAAA AGATTAAGGA TAGGAGTTGG TATGAGAGAT AATCATCTAC																	1380			
I	V	A	D	I	L	K	D	.						M	R	D	N	H	L	H
----->																				
ACACGTATTT TTCTATGAT TGTCAAACGG CATTGAGGA CTATATTAAT GGTTTACAG																	1440			
T	Y	F	S	Y	D	C	Q	T	A	F	E	D	Y	I	N	G	F	T	G	
GTGAATTAT CACGACAGAA CATTGGATT TATCAAATCC TTACACCGGT CAAGACGATG																	1500			
E	F	I	T	T	E	H	F	D	L	S	N	P	Y	T	G	Q	D	D	V	
TTCCTGATTA TAGTGCTTAT TGTAAAAAA TAGATTATCT TAATCAGAAA TATGGAAATC																	1560			
P	D	Y	S	A	Y	C	Q	K	I	D	Y	L	N	Q	K	Y	G	N	R	
GATTTAAAAA AGGAATTGAA ATCGGTTATT TTAAAGATAG GGAATCAGAT ATTTAGATT																	1620			
F	K	K	G	I	E	I	G	Y	F	K	D	R	E	S	D	I	L	D	Y	
ATTTAAAAAA TAAAGAATTG GATTTAAAAC TATTGTCAAT CCATCATAAT GGTAGGTATG																	1680			
L	K	N	K	E	F	D	L	K	L	L	S	I	H	H	N	G	R	Y	D	
ATTATCTGCA AGAAGAAGCT CTGAAAGTAC CAACAAAGGG AGCTTTAGC AGATTACTTT																	1740			
Y	L	Q	E	E	A	L	K	V	P	T	K	G	A	F	S	R	L	L	.	
AATCGTATGG AATTTGCCAT AGGCCGTGTG GAAGCGCACG TTTAGCTCA CTTTGATTAT																	1800			
GGTTTCGTA AGTTAAACTT AGATGTAGAA GATTTAAAC CGTTGAAAC GCAATTGAAG																	1860			
CGCATTTCGA TAAAGATGTT ATCTAAGGGG TTAGCTTTG AACTAAATAC CAAATCCCTT																	1920			

TATCTATATG GGAATGAAAA ACTTTATCGC TATGCTTAG AGATACTCAA ACAGCTTGGT 1980
 TGTAAACAAT ACTCTATAGG CTCTGACGGT CATATTCTG AACATTTTG TTATGAATTT 2040
 GATAGACTTC AAGGTCTGCT AAAGGACTAT CAAATTGATG AAAATCATT GATATGAGGA 2100
 AATTTTGAT AAAAAAGCTA GGCAATATTG CTTAGCTTT TTGTAATGCT ATTGATAGTT 2160
 TTAGTGAAAA TTTCAAAAAA ATAAAGAAAT CATTACTTG TTGCAAGCGC TTGCGTAAAT 2220
 TGTTATGATT TTATTGGTAA CAATTCATTA AAAAAGGAGA ATGATATGAA AAGAAAAGAC 2280
 M K R K D
 |---->
 TTATTTGGTG ATAAACAAAC TCAATACACG ATTAGAAAGT TAAGTGTGAG AGTAGCTTCA 2340
 L F G D K Q T Q Y T I R K L S V G V A S
 GTTACAACAG GGGTATGTAT TTTTCTTCAT AGTCCACAGG TATTTGCTGA AGAAGTAAGT 2400
 V T T G V C I F L H S P Q V F A E E V S
 GTTCTCCTG CAACTACAGC GATTGCAGAG TCGAATATTA ATCAGGTTGA CAACCAACAA 2460
 V S P A T T A I A E S N I N Q V D N Q Q
 TCTACTAATT TAAAAGATGA CATAAAACTCA AACTCTGAGA CGGTTGTGAC ACCCTCAGAT 2520
 S T N L K D D I N S N S E T V V T P S D
 ATGCCGGATA CCAAGCAATT AGTATCAGAT GAAACTGACA CTCAAAAGGG AGTGACAGAG 2580
 M P D T K Q L V S D E T D T Q K G V T E
 CCGGATAAGG CGACAAGCCT GCTTGAAGAA AATAAAAGTC CTGTTTCAGA TAAAAATACC 2640
 P D K A T S L L E E N K G P V S D K N T
 TTAGATTTAA AAGTAGCACC ATCTACATTG CAAAATACTC CCGACAAAAC TTCTCAAGCT 2700
 L D L K V A P S T L Q N T P D K T S Q A
 ATAGGTGCTC CAAGCCCTAC CTTGAAAGTA GCTAATCAAG CTCCACGGAT TGAAAATGGT 2760
 I G A P S P T L K V A N Q A P R I E N G
 TACTTTAGGC TACATCTTAA AGAATTGCTT CAAGGTCACTC CTGTTGAAAG CACTGGACTT 2820
 Y F R L H L K E L P Q G H P V E S T G L
 TGGATATGGG GAGATGTTGA TCAACCGTCT AGTAATTGGC CAAATGGTGC TATCCCTATG 2880
 W I W G D V D Q P S S N W P N G A I P M
 ACTGATGCTA AGAAAGATGA TTACGGTTAT TATGTTGATT TTAAATTATC TGAAAACAA 2940
 T D A K K D D Y G Y Y V D F K L S E K Q
 CGAAAACAAA TATCTTTTT AATTAATAAC AAAGCAGGGG CAAATTAAAG CGGCGATCAT 3000
 R K Q I S F L I N N K A G T N L S G D H
 CATATTCCAT TATTACGACC TGAGATGAAC CAAGTTGGG TTGATGAAAA GTACGGTATA 3060
 H I P L L R P E M N Q V W I D E K Y G I
 CATACTTATC AACCCCTCAA AGAAGGGTAT GTCCGTATTA ACTATTTGAG TTCCTCTAGT 3120
 H T Y Q P L K E G Y V R I N Y L S S S S
 AACTATGACC ACTTATCAGC ATGGCTCTT AAAGATGTTG CAACCCCYTC AACAACTTGG 3180
 N Y D H L S A W L F K D V A T P S T T W
 CCAGATGGTA GTAATTTGT GAATCAAGGA CTATATGGAA GGTATATTGA TGTATCACTA 3240
 P D G S N F V N Q G L Y G R Y I D V S L

AAAACTAACG CCAAAGAGAT TGGTTTTCTA ATCTTAGATG AAAGTAAGAC AGGAGATGCA 3300
 K T N A K E I G F L I L D E S K T G D A

 GTGAAAGTTC AACCCAACGA CTATGTTTT AGAGATTTAG CTAACCATAA CCAAATTTT 3360
 V K V Q P N D Y V F R D L A N H N Q I F

 GTAAAAGATA AGGATCCAAA GGTTTATAAT AATCCTTATT ACATTGATCA AGTGCAGCTA 3420
 V K D K D P K V Y N N P Y Y I D Q V Q L

 AAGGATGCC CACAAATTGA TTTAACAAAGT ATTCAAGCAA GTTTACAAC TCTAGATGGG 3480
 K D A Q Q I D L T S I Q A S F T T L D G

 GTAGATAAAA CTGAAATTTC AAAAGAATTG AAAGTGAAGT ATAAAAATCA AAATGCTATA 3540
 V D K T E I L K E L K V T D K N Q N A I

 CAAATTTCTG ATATCACTCT CGATACTAGT AAATCTTT TAATAATCAA AGGCGACTTT 3600
 Q I S D I T L D T S K S L L I I K G D F

 AATCTAAAC AAGGTCAATT CAACATATCT TATAATGGTA ACAATGTCAT GACAAGGCAA 3660
 N P K Q G H F N I S Y N G N N V M T R Q

 TCTTGGGAAT TAAAGACCA ACTTTATGCT TATAGTGGAA ATTTAGGTGC AGTTCTCAAT 3720
 S W E F K D Q L Y A Y S G N L G A V L N

 CAAGATGGTT CAAAAGTTGA AGCCAGCCTC TGGTCACCGA GTGCTGATAG TGTCACTATG 3780
 Q D G S K V E A S L W S P S A D S V T M

 ATTATTTATG ACAAAAGATAA CCAAAACAGG GTTGTAGCGA CTACCCCCCT TGTGAAAAAT 3840
 I I Y D K D N Q N R V V A T T P L V K N

 AATAAAAGGTG TTTGGCAGAC GATACTTGAT ACTAAATTAG GTATTAAAA CTATACTGGT 3900
 N K G V W Q T I L D T K L G I K N Y T G

 TACTATTATC TTTACGAAAT AAAAAGAGGT AAGGATAAGG TTAAGATTT AGATCCTTAT 3960
 Y Y Y L Y E I K R G K D K V K I L D P Y

 GCAAAGTCAT TAGCAGAGTG GGATAGTAAT ACTGTTAATG ATGATATTAA AACGGCTAAA 4020
 A K S L A E W D S N T V N D D I K T A K

 GCAGCTTTG TAAATCCAAG TCAACTTGGA CCTCAAAATT TAAGTTTGC TAAAATTGCT 4080
 A A F V N P S Q L G P Q N L S F A K I A

 AATTTAAAG GAAGACAAGA TGCTGTTATA TACGAAGCAC ATGTAAGAGA CTTCACTTCT 4140
 N F K G R Q D A V I Y E A H V R D F T S

 GATCGATCTT TGGATGGAAA ATTAAAAAT CAATTTGGTA CCTTGCAGC CTTTCAGAG 4200
 D R S L D G K L K N Q F G T F A A F S E

 AAACTAGATT ATTTACAGAA ATTAGGAGTT ACACACATTC AGCTTTTACC GGTATTGAGT 4260
 K L D Y L Q K L G V T H I Q L L P V L S

 TATTTTATG TTAATGAAAT GGATAAGTCA CGCTAACAG CTTACACTTC CTCAGACAAAT 4320
 Y F Y V N E M D K S R S T A Y T S S D N

 AATTACAATT GGGGCTATGA CCCACAGAGC TATTTGCTC TTTCTGGGAT GTATTCAAGAG 4380
 N Y N W G Y D P Q S Y F A L S G M Y S E

 AAACCAAAAG ATCCATCAGC ACGTATCGCC GAATTAAAAC AATTAATACA TGATATTCA 4440
 K P K D P S A R I A E L K Q L I H D I H

AAACGTGGCA	TGGGGGTTAT	ACTTGATGTC	GTCTATAATC	ACACTGCAAA	AACTTATCTC	4500
K R G M	G V I	L D V	V Y N H	T A K	T Y L	
TTTGAGGATA	TAGAACCTAA	TTATTATCAC	TTTATGAATG	AAGATGGTTC	ACCAAGAGAA	4560
F E D I	E P N	Y Y H	F M N E	D G S	P R E	
AGTTTTGGAG	GGGGACGTTT	AGGAACCACT	CATGCAATGA	GTCGTCGTGT	TTTGGTTGAT	4620
S F G G	G R L	G T T	H A M S	R R V	L V D	
TCCATTAAT	ATCTTACAAG	TGAATTAAA	GTTGATGGTT	TCCGTTTGAT	TATGATGGGA	4680
S I K Y	L T S	E F K	V D G F	R F D	M M G	
GATCATGATG	CGGCTGCGAT	TGAATTAGCT	TATAAAGAAG	CTAAAGCTAT	TAATCCTAAT	4740
D H D A	A A I	E L A	Y K E A	K A I	N P N	
ATGATTATGA	TTGGTGAGGG	CTGGAGAAC	TTCCAAGGCG	ATCAAGGTCA	GCCGGTTAAA	4800
M I M I	G E G	W R T	F Q G D	Q G Q	P V K	
CCAGCTGACC	AAGATTGGAT	GAAGTCAACC	GATACAGTTG	GCGCTTTTC	AGATGATATT	4860
P A D Q	D W M	K S T	D T V G	V F S	D D I	
CGTAATAGCT	TGAAATCTGG	TTTCCAAAT	GAAGGTACTC	CAGCTTCAT	CACAGGTGGC	4920
R N S L	K S G	F P N	E G T P	A F I	T G G	
CCACAATCTT	TACAAGGTAT	TTTTAAAAAT	ATCAAAGCAC	AACCTGGGAA	TTTTGAAGCA	4980
P Q S L	Q G I	F K N	I K A Q	P G N	F E A	
GATTGCCAG	GAGATGTGGT	GCAGTATATT	GCTGCACATG	ATAACCTTAC	CTTGCATGAT	5040
D S P G	D V V	Q Y I	A A H D	N L T	L H D	
GTGATTGCAA	AATCAATT	(SEQ ID NO:22)				5058
V I A K	S I .					

FIG. 4a

NLKAELSVED	EQYTATVYWK	SAHGSTPQEG	VNGATYLALY	LSQFDFEGPA	50
RAFLDVTANI	IHEDFSGEKL	GVAYEDDCMG	PLSMNAGVFQ	FDETNDNTI	100
ALNFRYPQGT	DAKTIQTKLE	KLNGVEKVTL	SDHEHTPHYV	PMDDELVSTL	150
LAVYEKQTGL	KGHEQVIGGG	TFGRLLERGV	AYGAMFPGDE	NTMHQANEYM	200
PLENIFRSAA	IYAEAIYELI	K	(SEQ ID NO:23)		221

FIG. 4b

MTDLEKIIKA	IKSDSQNQNY	TENGIDPLFA	APKTARINIV	GQAPGLKTQE	50
ARLYWKDKSG	DRLRQWLGV	EETFYHSGKF	AVLPLDFYYP	GKGKSGDLPP	100
RKGFAEKWHP	LILKEMPNVQ	LTLLVGQYAQ	KYYLGSSAHK	NLTETVKAYK	150
DYLPDYLPLV	HPSPRNQIWL	KKNPWFEKDL	IVDLQKIVAD	ILKD	194
(SEQ ID NO:24)					

FIG. 4c

MRDNHLHTYF SYDCQTAFED YINGFTGEFI TTEHFDSLNP YTGQDDVPDY	50
SAYCQKIDYL NQKYGNRFKK GIEIGYFKDR ESDILDYLKN KEFDLKLLSI	100
HHNGRYDYLQ EEALKVPTKG AFSRLL (SEQ ID NO:25)	126

FIG. 4d

MKRKDLFGDK QTQYTIRKLS VGVASVTTGV CIFLHSPQVF AEEVSVSPAT	50
TAIAESNINQ VDNQQSTNLK DDINSNSETV VTPSDMPDTK QLVSDETDTQ	100
KGVTEPDKAT SLLEENKGPV SDKNTLDLKVNAPSTLQNTPD KTSQAIGAPS	150
PTLKVANQAP RIENGYFRLH LKELPQGHPV ESTGLWIWGD VDQPSSNWPN	200
GAIPMTDAKK DDYGYYYVDFK LSEKQRKQIS FLINNKAGTN LSGDHHIPLL	250
RPEMNQVWID EKYGIHTYQP LKEGYVRINY LSSSSNYDHL SAWLFKDVAT	300
PSTTWPDGSN FVNQGLYGRY IDVSLKTNAK EIGFLILDES KTGDAVKVQP	350
NDYVFRDLAN HNQIFVKDKD PKVYNNPYYI DQVQLKDAQQ IDLTSIQASF	400
TTLDGVDKTE ILKELKVTDK NQNAIQISDI TLDTSKSLLI IKGDFNPKQG	450
HFNISYNGNN VMTRQSWEFK DQLYAYSGNL GAVLNQDGSK VEASLWSPSA	500
DSVTMIIYDK DNQNRVVATT PLVKNNKGW QTILDTKLGI KNYTGYYYLY	550
EIKRGKDKVK ILDPYAKSLA EWDSNTVNDD IKTAKAAFVN PSQLGPQNL	600
FAKIANFKGR QDAVIYEAHV RDFTSDRSLD GKLKNQFGTF AAFSEKLDYL	650
QKLGVTIQL LPVLSYFYVN EMDKSRSTAY TSSDNNYNWG YDPQSYFALS	700
GMYSEKPKDP SARIAELKQL IHDIHKRGMG VILDVVYNHT AKTYLFEDIE	750
PNYYHFMNED GSPRESFGGG RLGTTHAMSR RVLVDSIKYL TSEFKVDGFR	800
FDMMGDHAA AIELAYKEAK AINPNMIMIG EGWRTFQGDQ GQPVKPADQD	850
WMKSTDTVGV FSDDIRNSLK SGFPNEGTPA FITGGPQSLQ GIFKNIKAQP	900
GNFEADSPGD VVQYIAAHDN LTLHDVIAKS I (SEQ ID NO:26)	931

FIG. 4e

AATTCAAAGT	TTGACAGAAG	GTCAACTTCG	TTCTGATATC	CCTGAGTTCC	GTGCTGGTGA	60
I Q S	L T E G	Q L R	S D I	P E F R	A G D	
----->						
TAAGTGTACGT	GTTCACGCTA	AAGTTGTTGA	AGGTACTCGC	GAACGTATTG	AGATCTTG	120
T V R	V H A K	V V E	G T R	E R I Q	I F E	
AGGTGTTGTT	ATCTCACGTA	AAGGTCAAGG	AATCTCAGAA	ATGTACACAG	TACGTAAAAT	180
G V V	I S R K	G Q G	I S E	M Y T V	R K I	
TTCTGGTGGT	ATCGGTGTAG	AGCGTACATT	CCCAATTAC	ACTCCTCGTG	TTGATAAAAAT	240
S G G	I G V E	R T F	P I H	T P R V	D K I	
CGAAGTTGTT	CGTTATGGTA	AAGTACGTG	TGCTAAACTT	TACTACTTAC	GCGCATTGCA	300
E V V	R Y G K	V R R	A K L	Y Y L R	A L Q	
AGGTAAAGCT	GCACGTATTA	AAGAAATCCG	TCGTTAATTT	TGATGATCAG	ATTTTAAAAAA	360
TGCTTGGTTG	TTTGAGGATA	GTAACATATGT	TTTAAAACG	GACAACCAAG	ACGTAAAAAA	420
TCTGCCTGTG	GGCAGTTTT	TTACTAGGTC	CCCTTAGTTC	AATGGATATA	ACAACTCCCT	480
. H I Y C S G						
CCTAAGGAGT	AATTGCTGGT	TCGATTCCGG	CAGGGGACAT	ATTCAATTGCA	TGTAAATAGC	540
G L S	Y N S T	R N R	C P V	Y E N C	T F L	
GGTTTAGAGC	TATTTGCCCC	CAAATTTCTC	TGATTAAGTT	TATCGTTCT	ATCTTTTGT	600
P K S	S N Q G	L N R	Q N L	K D N R	D K Q	
TCTTGTAAATT	GATGTGCGTA	AACTTCTAAA	GTGATATTAA	AATTCTCGTG	ATCTAAAAC	660
E Q L	Q H A Y	V E L	T I N	L N E H	D L V	
TGAGAGATGG	AAATTAGATA	GCTTGCAAAT	GTATGCCTGA	GAGAGTGCAC	TCGTACCTCG	720
Q S I	S I L Y	S A F	T H R	L S H V	R V E	
CGACCAGTTA	TTTTCGGAT	AGTTTATTG	ACTGCATTAT	TTGAAAGTTT	GTCGAATAAT	780
R G T	I K R I	T K N	V A N	N S L K	D F L	
CTGTCGTTT	TATTTTTGT	AAATTCAATGC	AAAAAAAATA	ATGTATCATT	GTCAATTGGT	840
R D N	K N K T	F E H	L F F	L . T	D N D I P	
ATATTTCTGA	TACTACTTT	GTTTTTGTT	GGCAGGTATC	TTTGGTTGAA	ATGATAATCC	900
I N R	I S S K	N K T	P L Y	R Q N F	H Y D	
CAAGTTTAT	TAATTGATAA	ATATTGTTA	GTGTAATCAA	TATCATTAAAC	TGTTAACCT	960
W T K	N I S L	Y K N	T Y D	I D N V	T L G	
AAACATTCAG	CGAAGCGCAT	GCCAGTTTA	GCGATGAGGT	ATAACGCTGC	ATACGATTGA	1020
L C E	A F R M	<-----				
TGTTGTGATT	TTTCTTACA	AATTTTATC	AAGCGTAAGT	ATTCAATTGGT	TTCAAGAAAT	1080
TTTATCTCTA	TTTACGCC	TTATTTTG	CTTTAACCTT	AGTGAATAAA	CAAAATTTT	1140
TTTCTATATA	TCCCTCGTGA	ACAGCCATGG	ATACGCAGGC	TTTACATGT	ATGTTAAAAC	1200
GCTTTACTGT	ATCTTGCACA	TGCGTTGAC	TATAATGATT	TATGACTTGT	TGATATTTAG	1260

TGGAAGTAAT ATTGCAAAGT AATATATTTC CTATTATATG TTTATACGAT ATTCGATATT 1320
 CCCACCCGTT GTCGCGTTA CGGAAATACG CCATTGATAT ACTCCACATT AGCTAAAGAA 1380
 CAGGGTGTTC AAGGCTACCT TGATGGAAAA GGCTCTCTTA GAGATATTG TAAATGGTAT 1440
 GATATCTCAA GTCGCTCTGT TCTCCAAAAG TGGATAAAAC GGTATACTAG TGGTGAAGAC 1500
 TTGAAAGCCA CTAGTAGAGG ATATAGCCGT ATGAAACAAG GAAGGCAAGC CACATTTGAA 1560
 GAACGTGTAG AGATTGTTAA CTACACCATT GCCCATGGGA AAGACTATCA AGCAGCTATT 1620
 GAGAAGTTG GTGTTTCCTA CCAACAAATT TATTCTGGG TGCGTAAGCT TGAGAAGAAT 1680
 GGCTCACAAG GTTGGTTGA TAGACGTGTG AAAGGGTTGG AGAGTAGGCC TGATTTAAC 1740
 GAGATTGAGC AACTTTAAGT CAAGATTAAA CAATTGGAGG AACGTAATCG TCTCTTAGAA 1800
 ATCGAGGTTA GTTTACTAAA AAAGTTAGAA GACATCAAAC GAGGAAACAG ACGGTAAGAC 1860
 TAGGTAAGCA TTTAGCGGAG TTCCAAGTAA TCAAGAATTAA TTACGATGAG GAATCTAATG 1920
 TGCCTATTCA GCCCTTATGC CAACTCTTGA AGGGGTCTCG TTCAGGCTAT TACAAGTGGC 1980
 TCAATCGTCA AAAACAGAT TTTGAGACAA AAAATACAAA GCTAATGGCT AAAATCAAGG 2040
 AACTTCGTAG ACTCTACAAT GGTATCTTAG GTTATCGCCG TATGACAACA TTTATTAATC 2100
 GTCAACTTGG GACAACCTAA ACAAGAAC GGATTCGTTG ATTGATGAAC ATTCTGGGA 2160
 TTAGTTCAAGT CATTGTCGT GTTAGCCATG CTTGTACAAA AGCTGGTGAC AGATTTACG 2220
 AAGAAAATAT TCTTAATCGT GAATTACAG CCACAGCTCA TAACCAGAAA TGGTGCACAG 2280
 ATGTCACCTA TCTTCATAAC GGTCTGGAG CTAAAGCTTA TCTCAGTGCG ATTAAAGACC 2340
 TGTATAACGG TTCTATTATC GCTTATGAGA TTAGTCACAA CAATGAAATC CACTTGTAT 2400
 GAAGACCATT AAAAAGGGGC TAGAGCTCAA TCCAGGAGCC ACACCTATCA TCCATAGCGA 2460
 TTGAGGTAGT CAATATACTT CCAAAGAATA CCGTTATATC ATACAACAAG CTGGTCTGAC 2520
 CTTATCCATG TCCCGGATTG GCAAATGTAT TGATAATGCA CCAACTGAAA GTTTCTTGG 2580
 GTTTTCAAG ACTGAGTCTT ACCACCTTAA GAAATACAAC TCTTATGATG AGTTGGTCAA 2640
 TGATGTGGCA CGTTATATCG AATTCTACAA CACACAACGT TATCAATCAA AATTAAACAA 2700
 CCTGACTCCT CTAGAATTCA GGAATCAGGT TGCATAACTT ATCTTTATT ATTTGACTGT 2760
 CTACTTGACA GGGAGCCGTT CAGATTGCTT AACCTTCTA AATTGCTAA AATAGCTACA 2820
 AGAAAACGAG CCATTTAATG CTTATTCTT ATACTGTCTT GCCTCACGCT CTCCTCGACC 2880
 AAAAATTGAG CGTGAGGCTT TTTGTTCAT TAAACGATGA TATTTCCATA TTCATCAGTT 2940
 TGTTTCCGA GAGCCATCAA AGCTTCGATA AGGTCGATAA TTCCAGGAAT AAAGGTAATA 3000
 CTAAAAATAA TATATAAAAAA AACCTGGCCT ATTTTCCCTG CGTAAAATTT ATGCGCTCCA 3060
 ATGCCGCCCA AAAGAACGTT AATAAAACAT AAACTACTAT GTTAGCATAA GACTTTATTT 3120

TTACAACTGA ATTCATATA AATGGATTAG AGTAAGGGAT AAAAGAAATT AGCATAGCTC 3180
 TTTTGAATTA AAAAAAATTA ATATAATATG GAAAAAATTT TATTCATAA ACGTTTCATA 3240
 AAAGGTATGT AATCTAGTAT TTAGGCAACA CTATTTGTC ACTGGTGTCT AGTAACTTAT 3300
 AGATTGATAA TTTTACTAGT AAACGTAATT CTCGCTTTA AGAGTTAAAT GTCTATTAT 3360
 TGTAAGCTAA ATTGGGAGGT GAACTTATGT AAAATTAGAT AGGTACTGTC AAGTACGGGA 3420
 TGATTATTGA AACAGCCAGT ATGCATCATA AAATCTGTAT TGCTTAATAA CTATTCCTT 3480
 AACCAGACAT CAGTCATTG TTTATCATCG CTACCCCTAAG TCTAGTTTT TCAATAGAGC 3540
 ATTAGGTAGT TTTGATAAT AAAACTATAT AAACATGAGA ATTAGATTTC GTATTGCATT 3600
 CTTCATAATG AGTTATTGTA GATTTCCCTT TGAATAAATA GATACGAAAT TCAGTAACCT 3660
 CATATATAAA CGGCTCTATC ATTGAGATAG TTTGTCAAAT GAAGAAATT TTAATGGAAA 3720
 TAGTTTAAA AACATTAGTT GTAGGCGATG TAAAAATATT AATCCAGTGG ATGCAATAGT 3780
 TGCAGGAGTAA AAATAGAGAG GAGTAATTAG GAAGTGATAA AAAATGCTAT AGCATATATT 3840
 ACCAGAAAAA AAAATAGAAC ACTTATTATA TTTGCTATT TAAACAATTGT TCTTTCTTGC 3900
 TTGTATTCAAT GTTTAACAAAT AATGAAATCA AGTAATGAAA TAGAAAAGGC TTTATATGAA 3960
 M K S S N E I E K A L Y E
 |---->
 AGTTCTAATT CTTCAATATC AATTACAAAA AAAGATGGTA AATATTTAA TATTAATCAA 4020
 S S N S S I S I T K K D G K Y F N I N Q
 TTTAAGAATA TTGAAAAAAT AAAAGAGGTT GAAGAAAAAA TATTCATAA TGATGGATTA 4080
 F K N I E K I K E V E E K I F Q Y D G L
 GCAAAATTGA AAGATCTTAA AGTAGTTAGT GGTGAGCAAA GTATAAATAG AGAAGATTTA 4140
 A K L K D L K V V S G E Q S I N R E D L
 TCTGACGAAT TAAAAAATGT TGTTCACTA GAAGCTACAA GTAATACTAA AAGAAATCTT 4200
 S D E F K N V V S L E A T S N T K R N L
 TTATTTAGTA GTGGAGTATT TAGTTTAAA GAAGGAAAAA ATATAGAAGA AAATGATAAG 4260
 L F S S G V F S F K E G K N I E E N D K
 AATTCAATTG TTGTTCATGA AGAATTGCT AAACAAAACA AACTAAAATT GGGTGATGAA 4320
 N S I L V H E E F A K Q N K L K L G D E
 ATTGATCTTG AATTACTAGA TACGGAAAAA AGTGGAAAAA TAAAAAGTCA TAAATTTAAA 4380
 I D L E L L D T E K S G K I K S H K F K
 ATTATAGGAA TCTTTCTGG TAAAAAACAG GAAACATATA CAGGATTATC ATCTGATTT 4440
 I I G I F S G K K Q E T Y T G L S S D F
 AGCGAAAATA TGGTTTTGT AGATTATTCA ACTAGCCAAG AAATATTAAA TAAATCAGAG 4500
 S E N M V F V D Y S T S Q E I L N K S E
 AATAATAGAA TTGCAAATAA AATTTAATG TATTCTGGTA GTTTAGAATC TACAGAGCTT 4560
 N N R I A N K I L M Y S G S L E S T E L
 GCCTTAAACA AATTGAAAGA CTTTAAAATT GATAAGTCAA AGTATTCTAT TAAGAAAGAT 4620

A	L	N	K	L	K	D	F	K	I	D	K	S	K	Y	S	I	K	K	D				
AATAAAAGCAT	TCGAAGAGTC	TTTAGAGTCA	GTGAGTGGAA	TAAAACATAT	AATTAAAATA															4680			
N	K	A	F	E	E	S	L	E	S	V	S	G	I	K	H	I	I	K	I				
ATGACTTATT	CGATTATGTT	AGGTGGAATA	GTTGTTCTT	CATTAATCTT	GATTCTATGG															4740			
M	T	Y	S	I	M	L	G	G	I	V	V	L	S	L	I	L	I	L	W				
TTAAGAGAAA	GAATTTATGA	AATAGGTATA	TTTTTATCTA	TTGGAACAAAC	TAAGATACAA															4800			
L	R	E	R	I	Y	E	I	G	I	F	L	S	I	G	T	T	K	I	Q				
ATTATAAGGC	AATTTATATT	TGAGTTAATA	TTCATATCAA	TACCAAGTAT	AATATCCTCC															4860			
I	I	R	Q	F	I	F	E	L	I	F	I	S	I	P	S	I	I	S	S				
TTATTTTAG	GGAATCTACT	ATTAAGAGTA	ATTGTAGAAG	GATTATTAA	CTCAGAGAAC															4920			
L	F	L	G	N	L	L	L	K	V	I	V	E	G	F	I	N	S	E	N				
TCAATGATT	TCGGTGGAAAG	TTTAATAAAT	AAAAGCAGTT	TTATGTTAAA	CATAACAACA															4980			
S	M	I	F	G	G	S	L	I	N	K	S	S	F	M	L	N	I	T	T				
CTTGCAGAAA	GTTATTTAAT	ATTAATAAGT	ATTATTGTTT	TATCAGTTGT	AATGGCCTCT															5040			
L	A	E	S	Y	L	I	L	I	S	I	I	V	L	S	V	V	M	A	S				
TCATTAATAT	TATTTAAGAA	ACCACAAGAA	ATATTATCAA	AAATAAGTTA	GGAGCAAATA															5100			
S	L	I	L	F	K	K	P	Q	E	I	L	S	K	I	S	.							
ATGGATATAT	TAGAAATAAA	GAATGTAAAT	TACAGTTACG	CAAATTCTAA	AGAAAAAGTT															5160			
M	D	I	L	E	I	K	N	V	N	Y	S	Y	A	N	S	K	E	K	V				
TTGTCAGGAG	TAAATCAAAA	ATTTGAACTT	GGAAAGTTTT	ATGCGATAGT	AGGGAAAGTC															5220			
L	S	G	V	N	Q	K	F	E	L	G	K	F	Y	A	I	V	G	K	S				
GGAACAGGAA	AATCCACACT	TCTTCCTTA	CTTGCAGGAC	TTGATAAAAGT	TCAAACAGGA															5280			
G	T	G	K	S	T	L	L	S	L	L	A	G	L	D	K	V	Q	T	G				
AAAAATCTTGT	TTAAGAATGA	AGATATAGAA	AAGAAAGGAT	ATAGTAATCA	CAGAAAAAAAT															5340			
K	I	L	F	K	N	E	D	I	E	K	K	G	Y	S	N	H	R	K	N				
AATATATCTT	TGGTATTTCA	AAATTATAAT	TTAATAGATT	ATTTATGCC	GATTGAAAAT															5400			
N	I	S	L	V	F	Q	N	Y	N	L	I	D	Y	L	S	P	I	E	N				
ATTAGACTAG	TAAATAAAC	AGTAGATGAG	AGTATCTTGT	TCGAATTAGG	TTTAGATAAA															5460			
I	R	L	V	N	K	S	V	D	E	S	I	L	F	E	L	G	L	D	K				
AAACAAATAA	AAAGAAATGT	TATGAAATTA	TCTGGTGGTC	AGCAACAAAG	GGTAGCTATT															5520			
K	Q	I	K	R	N	V	M	K	L	S	G	G	Q	Q	Q	R	V	A	I				
GCTAGGGCAC	TGGTATCAGA	TGCCCAATA	ATACTAGCTG	ATGAGCCTAC	CGGTAACCTA															5580			
A	R	A	L	V	S	D	A	P	I	I	L	A	D	E	P	T	G	N	L				
GACAGTGT	TA	CTGCTGGAGA	AATAATT	(SEQ ID NO:27)																			5607
D	S	V	T	A	G	E	I	I	.														

FIG. 5a

IQSLTEGQLR SDIPEFRAGD TVRVHAKVVE GTRERIQIFE GVVISRKGQG	50
ISEMYTVRKI SGIGVERTF PIHTPRVDKI EVVRYGKVRR AKLYYLRALQ	100
GKAARIKEIR R (SEQ ID NO:28)	111

FIG. 5b

MRFAECLGLT VNDIDYTNKY LSINKTWDYH FNQRYLPTKN KSSIRNIPID	50
NDTLFFLHEF TKNKNDRFLFD KLSNNAVNKT IRKITGREVR VHSLRHTFAS	100
YLISISQVLD HENLNITLEV YAHQLQEQQD RNDKLNQRNL GQNSSKPLFT	150
CNEYVPCRNR TSNYSLGGSC YIH (SEQ ID NO:29)	173

FIG. 5c

MKSSNEIEKA LYESSNSSIS ITKKDGKYFN INQFKNIEKI KEVEEKIFQY	50
DGLAKLKDLK VVSGEQSINR EDLSDEFKNV VSLEATSNTK RNLLFSSGVF	100
SFKEGKNIEE NDKNSILVHE EFAKQNLKLG DGEIDLELLD TEKSGKIKSH	150
KFKIIGIFSG KKQETYTGLS SDFSENMVVF DYSTSQEILN KSENNRIANK	200
ILMYSGSLES TELALNKLKD FKIDKSKEYI KKDNKAFEEES LESVSGIKHI	250
IKIMTYSIML GGIVVLSLIL ILWLRERIYE IGIFLSIGTT KIQIIRQFIF	300
ELIFISIPSI ISSFLGNLL LKVIVEGFIN SENSMIFGGS LINKSSFMLN	350
ITTLAESYLI LISIIVLSVV MASSLILFKK PQEILSKIS	389
(SEQ ID NO:30)	

FIG. 5d

MDILEIKNVN YSYANSKEKV LSGVNQKFEL GKFYAIVGKS GTGKSTLLSL	50
LAGLDKVQTG KILFKNEDIE KKGYSNHRKN NISLVFQNYN LIDYLSPIN	100
IRLVNKSVDE SILFELGLDK KQIKRNVMKL SGGQQQRVAI ARALVSDAPI	150
ILADEPTGNL DSVTAGEII (SEQ ID NO:31)	169

FIG. 5e

CATATGACAA TATTTTCAA AGTCTACATC ACTTACTCGC CTGTCGTGGA AAATCTGGCA	60
ATACATTAAT CGACCAATTA GTTGCTGATG GTTACTTCA TGCGATAAT CACTACCATT	120
TTTCAATGG GAAGTCTCTG GCCACTTCATA ATACTAACCA ATTGATTGCGC GAAGTTGTCT	180
ATGTTGAAAT ATCCTTAGAT ACTATGTCTA GTGGTGAACA TGATTTAGTA AAAGTTAACAA	240
TTATCAGACC CACTACCGAG CATACTATCC CCACGATGAT GACAGCTAGC CCCTATCATC	300
AAGGTATCAA TGATCCTGCC GCAGACCAAA AAACATACCA AATGGAGGGT GCGCTAGCAG	360
TTAAACAGCC TAAACACATA CAAGTTGACA CAAAACCATT TAAAGAAGAA GTAAAACATC	420
CTTCAAAATT ACCCATCAGC CCTGCAACTG AAAGCTTCAC ACACATTGAC AGTTATAGTC	480
TCAATGACTA TTTCTTTCT CGTGGTTTG CTAATATATA CGTTTCAGGT GTGGGTACTG	540
CTGGCTCTAC GGGTTTCATG ACCAGTGGGG ATTACCAACA AATACAAAGC TTTAAAGCAG	600
TCATTGATTG GTTAAATGGT AAGGTTACTG CATTACAAG TCATAAACGA GATAAACAAAG	660
TCAAGGCTGA TTGGTCAAAC GGCCCTGTAG CAACCACAGG TAAATCTTAT CTCGGTACCA	720
TGTCAACTGG TTTAGCAACA ACTGGCGTTG AGGGGCTGAA AGTCATTATC GCTGAAGCCG	780
CAATCTCCAC ATGGTATGAT TATTATCGAG AAAATGGCT TGTGTGTAGT CCAGGCGGCT	840
ACCCCGGTGA AGATTTAGAC GTTTAACAG AATTAACATA CTCACGAAAC CTCTTAGCTG	900
GTGATTACAT CAAAAACAAAC GATTGCTATC AAGCATTGTT AAATGAACAA TCAAAAGCAA	960
TTGACCGTCA AAGTGGGAT TACAACCAAT ACTGGCATGA CCGTAATTAC CTAACTCACG	1020
TCAATAATGT CAAAAGTCGA GTAGTTTACA CTCATGGACT ACAGGATTGG AATGTTAACG	1080
CAAGACATGT CTACAAAGTT TTCAATGCAT TGCCCTAAAC CATCAAAAAA CACCTTTTT	1140
TACATCAAGG TCAACATGTG TATATGCATA ATTGGCAGTC GATTGATTT CGTGAAAGCA	1200
TGAATGCCTT ACTAAGCCAA GAACTACTTG GCATTGACAA TCATTTCCAA TTAGAAGAGG	1260
TCATTGGCA AGATAATACT ACTGAGCAAA CTTGGCAAGT TTTAGATGCT TTCGGAGGAA	1320
ACCATCAAGA GCAAATTGGT TTAGGTGATA GTAAAAAAACT TATTGATAAC CATTATGACA	1380
AAGAACCTT TGATACTTAT TGAAAGACT TCAATGTGTT CAAAAATGAT CTTTTCAAGG	1440
GAAATAATAA AACCAATCAA ATCACTATTA ATCTTCCTCT AAAGAAAAAT TATCTCCTGA	1500
ATGGACAGTG CAAACTCCAT CTACGTGTTA AAAACTAGTGA CAAAAAGGCC ATTTTATCAG	1560
CCCAAATCTT AGACTATGGT CCTAAAAAAC GATTCAAAGA TACACCAACC ATCAAATTCT	1620
TAAACAGCCT TGATAATGGT AAAAATTTG CCAGAGAACG TTTACGTGAA CTCCCGTTA	1680
CTAAAGATCA TTATCGTGTG ATCAGTAAAG GTGTCTTGAA CCTTCAAAAT CGTACAGACT	1740
TACTTACAAT TGAGGCTATC GAGCCAGAAC AATGGTTGAA TATCGAGTTT AGCCTCCAAC	1800
CAAGTATATA TCAATTGAGT AAAGGTGATA ATCTAAGGAT TATCCTTTAT ACAACTGATT	1860
TTGAACATAC CATTGAGAT AATGCTAGTT ACTCTATAAC AGTAGATTTG AGTCAATCTT	1920
ATTTAACTAT CCCAACTAAT CAAGGAAATT AACTTATGAA ACTTCTTACT AAAGAACGGT	1980
TTGATGATTC TCAACACTTT TGGTACCAAGA TCAATTATT ACAAGAGAGT AACTTCGGAG	2040
CAGTTTTGA CCATGATAAT AAAAACATTC CACAGGTTGT TGCAACTATT GTTGATGATT	2100
TACAAGGTTTC CGGAAGTTCG AATCATTCT GGTATTTGG CAATACTACT GATACTTCCA	2160
TCCTTATGAT TGCTCATTAA AATCGAAAAT TCTATATTCA GGTAAATTAA AAGGACTTTG	2220
ACTTTGCAC TCAATTAAATA GCTATAAAATA ATTGGAAGAG TCTCCTCCAA ACTCAACTTG	2280
AAGCTCTAAA CGATACCCCTA GCAATATTTC AATAAATAAG GTAGAATGGA GTGACAAAGC	2340
AACGCGAGGG AGACTGATTA ATGTCATCTT ATTGGAATAA CTATCCTGAA CTTAAAAAAA	2400

ATATTGATGA AACCAATCAA CTAATTCAAG AAAGAATACA GGTCAGAAAT AAAGATATTG	2460
AAGCGGCGCT AAGCCAACTC ACAGCTGCGG GAGGAAAACA GCTCAGACCA GCATTCTTT	2520
ACCTTTTTC TCAACTTGGT AATAAGGAGA ATCAAGATAC TCAGCAACTA AAGAAAATCG	2580
CTGCTTCTTT AGAAATCCTT CACGTTGCTA CATTAAATCCA TGATGATGTC ATTGATGACT	2640
CACCACTAAG ACGTGGAAAT ATGACCATTG AAAGCAAGTT TGGCAAAGAC ATCGCAGTTT	2700
ATACTGGGA TTTACTTTTC ACAGTCTTT TCGATCTTAT TTTAGAATCT ATGACTGATA	2760
CACCATTTAT GAGGATTAAT GCAAAATCTA TCGGTAAAAT TCTCATGGGA GAATTGGACC	2820
AGATGCACCT TCGTTACAAT CAACACAAG GTATCCATCA CTATTTACGT GCGATTCAG	2880
GTAAGACAGC CGAACTCTTT AAATTAGCTA GCAAAGAAGG AGCTTACTTT GGTGGTGCAG	2940
AGAAGGAGGT TGTTCGTCTA GCAGGCCATA TCGGCTTAA CATTGGTATG ACATTCCAAA	3000
TTTTGGATGA TATCCTGGAT TATACTGCAG ATAAAAAAAC ATTTAATAAG CCTGTCTTAG	3060
AGGATTTAAC ACAAGGCCATT TACAGCCTTC CTCTACTTCT TGCCATTGAA GAAAATCCTG	3120
ATATTTCAA ACCTATTTA GATAAAAAAA CAGATATGGC TACTGAAGAC ATGGAAAAAA	3180
TTGCTTATCT CGTCGTTTCC CATAGAGGTG TTGACAAAGC TCGCCATCTA GCTCGTAAAT	3240
TTACTGAGAA AGCTATTAGT GACATAAATA AGCTACCCCA GAACTCTGCA AAAAAACAGT	3300
TGCTACAATT AACTAATTAC CTTTAAAAC GCAAAATTTA ATAATAAAA AAACATTCCA	3360
CAATGCTAGA AAAGCAGTTA GGGATGTT TTTTATTATC ATTATTTAT CGCACCTATC	3420
AATCATCATA GATCACCATC ATCAGCGGCT TTCAGCTGAC GGTAACGTTG ACTACTTGA	3480
GACAATTCTT GAGGAGAACCC TTCCAACCTCT AATTGCCAT TTTCTATAAA TAAGATACGA	3540
TCAGCATGTT CAATACCTT TAAGTGATGT GTAATCCAAA CTAAGGTCTT ACCTTCCAAT	3600
TCTTCATAA ATACCCTTAG TAAGGCTTGT TCAGTAATAG GATCAAGTCC AACAGTTGGC	3660
TCATCTAAGA TAACAATTGG GACATCTTT AGTAAGATTC TAGCCAAAGC AATTCTATGC	3720
CTTTCGCCAC CTGAAAACCT AAGTCCAGCT TCATCAACCA TTGTATAGAG ACCATCTGAT	3780
AAATCAGTGA CCATCTCTT CAATCCAAT CGTTCAAGAA CTTCCATAC ATCTTCTTCA	3840
CTAGCATCTT GGTTCCAAT GCGAATGTTA TTAGCAGGG TTGTATTAAA AAGGTAGGGC	3900
GCTTGTGTA TCACTCCAAT ATAGTTAGAA ATGCAATCAC CAACTATTGA AACATCAGCA	3960
CCGCCTAGGG TAATCTTCCC TTGACTTGCT TTCAAGTCGC CACGAAGTAG ACTAGCTAAG	4020
GTACTCTTGC CAGAACCACT CCGCCCTAAA ATAGCAATT TTTCTCCTTC TTTAATATCC	4080
AAATCTAAAT GATGCAAAAC CCATTTCTCT TGTGGCTTAT ACTGGAAACT TAAATTCTTG	4140
ACGGAAAAAT CATATGGCTT ATTAGGCAAT T (SEQ ID NO:32)	4171

FIG. 6a

YDNIFQSLHH	LLACRGKSGN	TLIDQLVADG	LLHADNHYHF	FNGKSLATFN	50
TNQLIREVVY	VEISLDTMSS	GEHDLVKVNI	IRPTTEHTIP	TMMTASPYHQ	100
GINDPAADQK	TYQMEGALAV	KQPKHIQVDT	KPFKEEVKHP	SKLPISPATE	150
SFTHIDSYSL	NDYFLSRGFA	NIYVSGVGTA	GSTGFMTSGD	YQQIQSFKAV	200
IDWLNGKVTA	FTSHKRDKQV	KADWSNGLVA	TTGKSYLGTM	STGLATTGVE	250
GLKVIIAEAA	ISTWYDYYRE	NGLVCSPGGY	PGEDLDVLTE	LTYSRNLLAG	300
DYIKNNDCYQ	ALLNEQSKAI	DRQSGDYNQY	WHDRNYLTHV	NNVKSRRVVT	350
HGLQDWNVKP	RHVYKVFNAL	PQTICKHLFL	HQGQHVYMHN	WQSIDFRESM	400
NALLSQELLG	IDNHFQLEEV	IWQDNTTEQT	WQVLDAGGGN	HQEIQIGLGD	450
KKLIDNHYDK	EAFDTYCKDF	NVFKNDLFKG	NNKTNQITIN	LPLKKNYLLN	500
GQCKLHLRVK	TSDKKAILSA	QILDYGPKKR	FKDTPTIKFL	NSLDNGKNFA	550
REALRELPFT	KDHYRVISKG	VNLQNRSDL	LTIEAIEPEQ	WFDIEFSLQP	600
SIYQLSKGDN	LRIILYTTDF	EHTIRDNASY	SITVDLSQSY	LTIPTNQGN	649
(SEQ ID NO:33)					

FIG. 6b

MKLLTKERFD	DSQHFWYQIN	LLQESNFGAV	FDHDNKNIPQ	VVATIVDDLQ	50
GSGSSNHFWY	FGNTTDTTSIL	MIAHLNRFY	IQVNLKDFDF	ALNLIAINNW	100
KSLLQTQLEA	LNDTLAIFQ	(SEQ ID NO:34)			119

FIG. 6c

MSSYWNNYPE	LKKNIDETNQ	LIQERIQVRN	KDIEAALSQL	TAAGGKQLRP	50
AFFYLFSQLG	NKENQDTQQL	KKIAASLEIL	HVATLIHDDV	IDDSPLRRGN	100
MTIQSKFGKD	IAVYTGDLF	TVFFDLILES	MTDTPFMRIN	AKSMRKILMG	150
ELDQMHLRYN	QQQGIHHYLR	AISGKTAELF	KLASKEGAYF	GGAEKEVVRL	200
AGHIGFNIGM	TFQILDDILD	YTADKTFNK	PVLEDLTQGV	YSLPLLLAIE	250
ENPDIFKPIL	DKKTDMATED	MEKIAVLVS	HRGVDKARHL	ARKFTEKAIS	300
DINKLPQNSA	KKQLLQLTNY	LLKRKI	(SEQ ID NO:35)		326

FIG. 6d

LPNKPYDFSV KNLSFQYKPO EKWVLHHLDL DIKEGEKIAI LGRSGSGKST 50
LASLLRGDLK ASQGKITLGG ADVSIVGDCI SNYIGVIQQA PYLFNTTLLN 100
NIRIGNQDAS EEDVWKVLER VGLKEMVTDL SDGLYTMVDE AGLRFSGGER 150
HRIALARILL KDVPIVILDE PTVGLDPITE QALLRVFMKE LEGKTLVWIT 200
HHLKGIEHAD RILFIENGQL ELEGSPQELS QSSQRYRQLK AADDGDL 247
(SEQ ID NO:36)

FIG. 6e

AATTCTATTT	GGAGGTTTT	CTTGAATAAA	TGGTTAGTTA	AGGCAAGTTC	CTTAGTTGTT	60
TTAGGTGGA	TGGTTTTATC	TGCGGGTTCC	CGAGTTTAG	CGGATACTTA	TGTCCGTCCA	120
ATTGATAATG	GTAGAATTAC	AACAGGTTTC	AATGGTTATC	CTGGACATTG	TGGGGTGGAT	180
TATGCTGTT	CGACTGGAAC	GATTATTAGG	GCAGTGGCAG	ATGGTACTGT	GAAATTGCA	240
GGAGCTGGAG	CCAACTTTTC	TTGGATGACA	GACTTAGCAG	GAAATTGTGT	CATGATTCAA	300
CATGCGGATG	GAATGCATAG	TGGTTACGCT	CATATGTCAC	GTGTGGTGGC	TAGGACTGGG	360
GAAAAAGTCA	AACAAGGAGA	TATCATCGGT	TACGTAGGAG	CAACTGGTAT	GGCGACGGGA	420
CCTCACCTTC	ATTTTGAATT	TTTACCAGCT	AACCCTAATT	TTCAAAATGG	TTTCCATGGA	480
CGTATCAATC	CAACGTCACT	AATTGCTAAC	GTTGCGACCT	TTAGTGGAAA	AACGCAAGCA	540
TCAGCTCCAA	GCATTAAGCC	ATTACAATCA	GCTCCTGTAC	AGAATCAATC	TAGTAAATTA	600
AAAGTGTATC	GAGTAGATGA	ATTACAAAAG	GTAAATGGTG	TTTGGTTAGT	CAAAAATAAC	660
ACCCCTAACGC	CGACTGGGTT	TGATTGGAAC	GATAATGGTA	TACCAAGCATT	AGAAATTGAT	720
GAGGGTGATG	CTAATGGTAA	TTTGACAGCT	GACCAGGTT	TTCAAAAAGG	TGGTTACTTT	780
ATCTTAATC	CTAAAACCT	TAAGACTGTA	GAAAACCCA	TCCAAGGAAC	AGCTGGTTA	840
ACTTGGGCTA	AGACACGCTT	TGCTAATGGT	AGTTCAGTTT	GGCTTCGCGT	TGACAACAGT	900
CAAGAACTGC	TTTACAAATA	GTGGAGGTA	TTGATTCAATT	GTAAATG	ACAGTTTGT	960
TACTAACTAA	GTACAATTTC	TTTAAACCGT	CTGAAAATAA	TTTATAGTC	CAGTAAAGTG	1020
TGATATTATA	GTCTCGGACT	AATAAAAAGG	AAATAGGAAT	TGAAGCAATG	AAAATGAATA	1080
AAAAGGTACT	ATTGACATCG	ACAATGGCAG	CTTCGCTATT	ATCAGTCGCA	AGTGTCAAG	1140
CACAAGAAC	AGATACGACG	TGGACAGCAC	GTACTGTTTC	AGAGGTAAAG	GCTGATTGG	1200
TAAAGCAAGA	CAATAAAATCA	TCATATACTG	TGAAATATGG	TGATACACTA	AGCGTTATTT	1260
CAGAAGCAAT	GTCAATTGAT	ATGAATGTCT	TAGCAAAAT	TAATAACATT	GCAGATATCA	1320
ATCTTATTAA	TCCTGAGACA	ACACTGACAG	TAACCTACGA	TCAGAAGAGT	CATACTGCCA	1380
CTTCAATGAA	AATAGAAACA	CCAGCAACAA	ATGCTGCTGG	TCAAACAACA	GCTACTGTGG	1440
ATTTGAAAAC	CAATCAAGTT	TCTGTTGCAG	ACCAAAAAGT	TTCTCTCAAT	ACAATTTCGG	1500
AAGGTATGAC	ACCAGAAAGCA	GCAACAACGA	TTGTTTCGCC	AATGAAGACA	TATTCTCTG	1560
CGCCAGCTTT	GAAATCAAAA	GAAGTATTAG	CACAAGAGCA	AGCTGTTAGT	CAAGCAGCAG	1620
CTAATGAACA	GGTATCAACA	GCTCCTGTGA	AGTCGATTAC	TTCAAGATT	CCAGCAGCTA	1680
AAGAGGAAGT	TAAACCAACT	CAGACGTCAG	TCAGTCAGTC	AACAACAGTA	TCACCAGCTT	1740
CTGTTGCCGC	TGAAACACCA	GCTCCAGTAG	CTAAAGTAGC	ACCGGTAAGA	ACTGTAGCAG	1800
CCCCTAGAGT	GGCAAGTGT	AAAGTAGTCA	CTCCTAAAGT	AGAAAACGGT	GCATCACCAG	1860
AGCATGTATC	AGCTCCAGCA	GTTCTGTGA	CTACGACTTC	AACAGCTACA	GACAGTAAGT	1920
TACAAGCGAC	TGAAGTTAAG	AGCGTTCCGG	TAGCACAAAA	AGCTCCAACA	GCAACACCGG	1980
TAGCACAAACC	AGCTTCAACA	ACAAATGCAG	TAGCTGCACA	TCTGAAAAT	GCAGGGCTCC	2040
AACCTCATGT	TGCAGCTTAT	AAAGAAAAAG	TAGCGTCAAC	TTATGGAGTT	AATGAATTCA	2100
GTACATACCG	TGCAGGTGAT	CCAGGTGATC	ATGGTAAAGG	TTTAGCAGTC	GACTTTATTG	2160
TAGGTTAAAAA	CCAAGCACTT	GGTAATGAAG	TTGCACAGTA	CTCTACACAA	AATATGGCAG	2220
CAAATAACAT	TTCATATGTT	ATCTGGCAAC	AAAAGTTTA	CTCAAATACA	AATAGTATT	2280
ATGGACCTGC	TAATACTTGG	AATGCAATGC	CAGATCGTGG	TGGCGTTACT	GCCAACCATT	2340
ATGACCATGT	TCACGTATCA	TTAACAAAT	AATATAAAA	AGGAAGCTAT	TTGGCTTCTT	2400

TTTTATATGC CTTGAATAGA CTTCAAGGT TCTTATCTAA TTTTTATTAA ATTGAGGAGA 2460
 TTAAGCTATA AGTCTGAAAC TACTTTCACG TTAACCGTGA CAAATCAAAC ACGTTAAAAC 2520
 TAAAATCTAA GTCTGTAAAG ATTATTGAAA ACGTTAAA AACAGATATA ATAAGGTTG 2580
 TAGATATCTA AAATTAAAAA AGATAAGGAA GTGAGAATAT GCCACATCTA AGTAAAGAAG 2640
 CTTTAAAAAA GCAAATAAAAA AATGGCATT TTGTGTCATG TCAAGCTTG CCTGGGGAGC 2700
 CTCTTATAC TGAAAGTGG A GTGTTATGC CTCTTTAGC TTTGGCAGCT CAAGAACAG 2760
 GAGCGGTTGG TATAAGAGCC AATAGTGTCC GCGACATTAA GGAAATTCAA GAAGTTACTA 2820
 ATTTACCTAT CATCGGCATT ATTAAACGTG AATATCCTCC ACAAGAACCA TTTATCACTG 2880
 CTACGATGAC AGAGGTGGAT CAATTAGCTA GTTTAGATAT TGCAAGTAATA GCCTTAGATT 2940
 GTACACTTAG AGAGCGTCAT GATGGTTGA GTGTAGCTGA GTTATTCAA AAGATAAAAG 3000
 GGAAATATCC TGAACAGTTG CTAATGGCTG ATATAAGTAC TTTGAAGAA GGTAAAAATG 3060
 CTTTGAAAGC AGGAGTTGAT TTTGTGGTA CAACTCTATC TGGATAACACA GATTACAGCC 3120
 GCCAAGAAGA AGGACCGGAT ATAGAACTCC TTAATAAGCT TTGTCAAGCC GGTATAGATG 3180
 TGATTGCGGA AGGTAAAATT CATACTCCTA AGCAAGCTAA TGAAATTAAT CATATAGGTG 3240
 TTGCAGGAAT TGTAGTTGGT GGTGCTATCA CTAGACCAAA AGAAATAGCG GAGCGTTCA 3300
 TCTCAGGACT TAGTTAAAAG TGTTACTCAA AAATCAAAAT CAAAATAAAA AAGGGGAATA 3360
 GTTATGAGTA TCAAAAAAAAG TGTGATTGGT TTTGCCTCG GAGCTGCAGC ATTATCAATG 3420
 TTTGCTTGTG TAGACAGTAG TCAATCTGTT ATGGCTGCCG AGAAGGATAA AGTCGAAATT 3480
 (SEQ ID NO:37)

FIG. 7a

NSIWRFFLNK WLVKASSLVV LGGMVLSAGS RVLADTYVRP IDNNGRITTGF 50
 NGYPGHCGVD YAVPTGTIIIR AVADGTVKFA GAGANFSWMT DLAGNCVMIQ 100
 HADGMHSGYA HMSRVVARTG EKVQGDIIG YVGATGMATG PHLHFEFLPA 150
 NPNFQNGFHG RINPTSLIAN VATFSGKTQA SAPSIKPLQS APVQNQSSKL 200
 KVYRVDELQK VNGVWLVKNN TLTPTGFDWN DNGIPASEID EVDANGNLTA 250
 DQVLQKGGYF IFNPKTLKTV EKPIQGTAGL TWAKTRFANG SSVWLRVDNS 300
 QELLYK (SEQ ID NO:38) 306

FIG. 7b

MKMNKKVLLT	STMAASLLSV	ASVQAQETDT	TWTARTVSEV	KADLVKQDNK	50
SSYTVKYGDT	LSVISEAMSI	DMNVLAKINN	IADINLIYPE	TTLTVTYDQK	100
SHTATSMKIE	TPATNAAGQT	TATVDLKTNQ	VSVADQKVSL	NTISEGMTPE	150
AATTIVSPMK	TYSSAPALKS	KEVLAQEQAQ	SQAAANEQVS	TAPVKSITSE	200
VPAAKEEVKP	TQTSVSQSTT	VSPASVAAET	PAPVAKVAPV	RTVAAPRVAS	250
VKVVTPKVET	GASPEHVSAP	AVPVTTTSTA	TDSKLQATEV	KSVPVAQKAP	300
TATPVAQPAS	TTNAVAAHPE	NAGLQPHVAA	YKEKVASTYQ	VNEFSTYRAG	350
DPGDHGKGGLA	VDFIVGKNQA	LGNEVAQYST	QNMAANNISY	VIWQQKFYSN	400
TNSIYGPANT	WNAMPDRGGV	TANHYDHVHV	SFNK	(SEQ ID NO:39)	434

FIG. 7c

MPHLSKEAFK	KQIKNGIIVS	CQALPGEPLY	TESGGVMPPLL	ALAAQEAGAV	50
GIRANSVRDI	KEIQEVTNLP	IIGIIKREYP	PQEPMFITATM	TEVDQLASLD	100
IAVIALDCTL	RERHDGLSVA	EFIQKIKGKY	PEQLLMADIS	TFEEGKNAFE	150
AGVDFVGTTL	SGYTDYXRQE	EGPDIELLNK	LCQAGIDVIA	EGKIHTPKQA	200
NEINHIGVAG	IVVGGAITRP	KEIAERFISG	LS	(SEQ ID NO:40)	232

FIG. 7d

MSIKKSVIGF	CLGAAALSMF	ACVDSSQSVM	AAEKDKVEI	39
(SEQ ID NO:41)				

FIG. 7e

ATGAAAATGA	ATAAAAAGGT	ACTATTGACA	TCGACAATGG	CAGCTTCGCT	50
ATTATCAGTC	GCAAGTGTTC	AAGCACAAGA	AACAGATACG	ACGTGGACAG	100
CACGTACTGT	TTCAGAGGTA	AAGGCTGATT	TGGTAAAGCA	AGACAATAAA	150
TCATCATATA	CTGTGAAATA	TGGTGATACA	CTAACCGTTA	TTTCAGAAGC	200
AATGTCAATT	GATATGAATG	TCTTAGCAAA	AATTAATAAC	ATTGCAGATA	250
TCAATCTTAT	TTATCCTGAG	ACAACACTGA	CAGTAACCTA	CGATCAGAAG	300
AGTCATACTG	CCACTTCAAT	GAAAATAGAA	ACACCAGCAA	CAAATGCTGC	350
TGGTCAAACA	ACAGCTACTG	TGGATTGAA	AACCAATCAA	GTTCCTGTTG	400
CAGACCAAAA	AGTTTCTCTC	AATACAATTI	CGGAAGGTAT	GACACCAGAA	450
GCAGCAACAA	CGATTGTTTC	GCCAATGAAG	ACATATTCTT	CTGCGCCAGC	500
TTTGAATCA	AAAGAAGTAT	TAGCACAAGA	GCAAGCTGTT	AGTCAAGCAG	550
CAGCTAATGA	ACAGGTATCA	ACAGCTCCTG	TGAAGTCGAT	TACTTCAGAA	600
GTTCCAGCAG	CTAAAGAGGA	AGTTAAACCA	ACTCAGACGT	CAGTCAGTCA	650
GTCAACAACA	GTATCACCAG	CTTCTGTTGC	CGCTGAAACA	CCAGCTCCAG	700
TAGCTAAAGT	AGCACCGGT	AGAACTGTAG	CAGCCCCTAG	AGTGGCAAGT	750
GTTAAAGTAG	TCACTCCTAA	AGTAGAAACT	GGTGCATCAC	CAGAGCATGT	800
ATCAGCTCCA	GCAGTTCTG	TGACTACGAC	TTCAACAGCT	ACAGACAGTA	850
AGTTACAAGC	GAATGAAAGTT	AAGAGCGTTC	CGGTAGCACA	AAAAGCTCCA	900
ACAGCAACAC	CGGTAGCACA	ACCAGCTTC	ACAACAAATG	CAGTAGCTGC	950
ACATCCTGAA	AATGCAGGGC	TCCAACCTCA	TGTTGCAGCT	TATAAAGAAA	1000
AAGTAGCGTC	AACTTATGGA	GTAAATGAAT	TCAGTACATA	CCGTGCAGGT	1050
GATCCAGGTG	ATCATGGTAA	AGGTTTAGCA	GTCGACTTTA	TTGTAGGTAA	1100
AAACCAAGCA	CTTGGTAATG	AAGTTGCACA	GTACTCTACA	CAAATATGG	1150
CAGCAAATAA	CATTTCATAT	GTTATCTGGC	AACAAAAGTT	TTACTCAAAT	1200
ACAAATAGTA	TTTATGGACC	TGCTAAACT	TGGAATGCAA	TGCCAGATCG	1250
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AATAA					1305

(SEQ ID NO:42)

FIG. 8

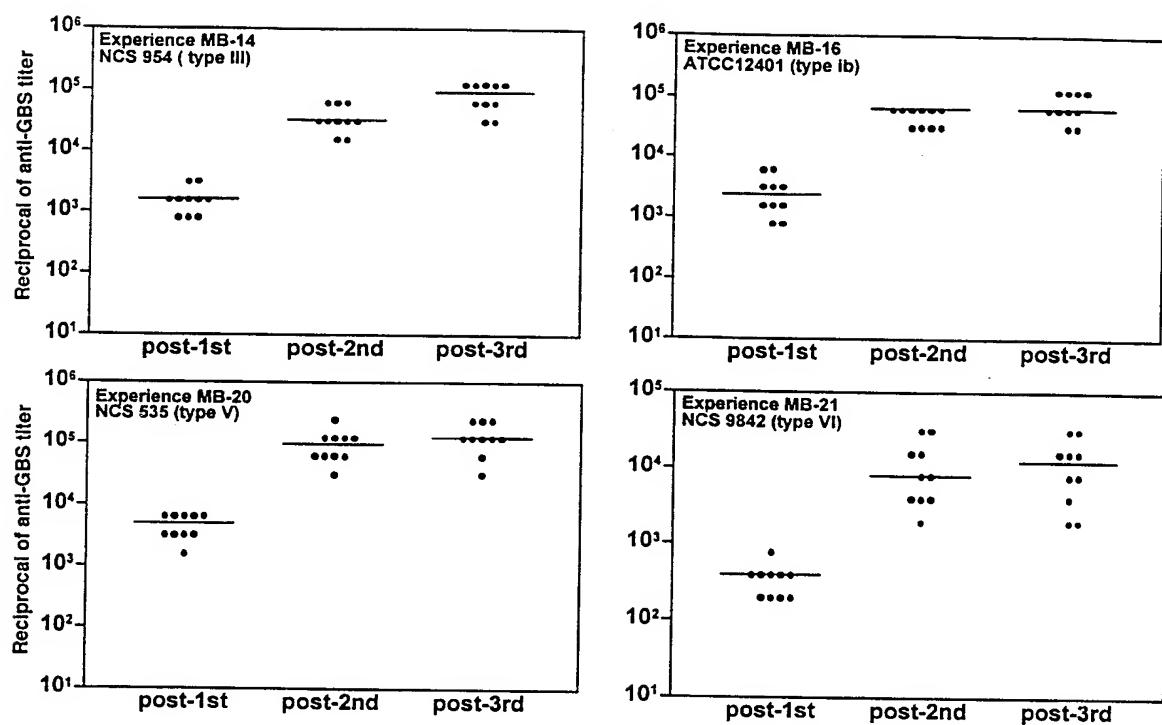
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ACGACTTCAA	CAGCTACAGA	CAGTAAGTTA	CAAGCGACTG	AAGTTAAGAG	800
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CTGGCAACAA	AAGTTTACT	CAAATACAAA	TAGTATTAT	GGACCTGCTA	1150
ATACTTGGAA	TGCAATGCCA	GATCGTGGTG	GCGTTACTGC	CAACCATTAT	1200
GACCATGTTG	ACGTATCATT	TAACAAATAA	(SEQ ID NO:43)		1230

FIG. 9

QETDTTWTAR	TVSEVKADLV	KQDNKSSYTV	KYGDTLSVIS	EAMSIDMNVL	50
AKINNIADIN	LIYPETTLTV	TYDQKSHTAT	SMKIETPATN	AAGQTTATVD	100
LKTNQSVVAD	QKVSLNTISE	GMTPEAATTI	VSPMKTYSSA	PALKSKEVLA	150
QEQAQSQAAA	NEQVSTAPVK	SITSEVPAAK	EEVKPTQTSV	SQSTTVSPAS	200
VAAETPAPVA	KVAPVRTVAA	PRVASVKVVT	PKVETGASPE	HVSAPAVPVT	250
TTSTATDSKL	QATEVKSVPV	AQKAPTATPV	AQPASTTNAV	AAHPENAGLQ	300
PHVAAYKEKV	ASTYGVNEFS	TYRAGDPGDH	GKGLAVDFIV	GKNQALGNEV	350
AQYSTQNMAA	NNISYVIWQQ	KFYSNTNSIY	GPANTWNAMP	DRGGVTANHY	400
DHVHVSFNK	(SEQ ID NO:44)				409

FIG. 9a

Fig. 10



SEQUENCE LISTING

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<120> NOVEL GROUP B STREPTOCOCCUS ANTIGENS

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Phe Ala Val Gln Phe Ile Gly Leu Lys Pro Asp Tyr Pro Gly Lys Thr	
35 40 45	
tac ttt att atc cta ttg aca gca tgg act ttg atg gca tta gta act	191
Tyr Phe Ile Ile Leu Leu Thr Ala Trp Thr Leu Met Ala Leu Val Thr	
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Ala Leu Val Gly Trp Asp Asn Arg Tyr Gly Ser Phe Leu Ser Leu Leu	
65 70 75	
ata tta tta ttc cag ctt ggt tca agc gca gga act tac cca ata gaa	287
Ile Leu Leu Phe Gln Leu Gly Ser Ser Ala Gly Thr Tyr Pro Ile Glu	
80 85 90 95	
ttg agt cct aag ttc ttt caa aca att caa cca ttt tta ccg atg act	335
Leu Ser Pro Lys Phe Phe Gln Thr Ile Gln Pro Phe Leu Pro Met Thr	
100 105 110	
tac tct gtt tca gga tta aga gag acc atc tcg ttg acg gga gac gtt	383
Tyr Ser Val Ser Gly Leu Arg Glu Thr Ile Ser Leu Thr Gly Asp Val	
115 120 125	
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Asn His Gln Trp Arg Met Leu Val Ile Phe Leu Val Ser Ser Met Ile	
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Leu Ala Leu Leu Ile Tyr Arg Lys Gln Glu Asp	
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Met Ser Thr	
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Leu Thr Ile Ile Ala Thr Leu Thr Ala Leu Glu His Phe Tyr Ile	
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Met Tyr Leu Glu Thr Leu Ala Thr Gln Ser Asn Met Thr Gly Lys Ile	
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Phe Ser Met Ser Lys Glu Glu Leu Ser Tyr Leu Pro Val Ile Lys Leu	
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Phe Lys Asn Gln Gly Val Tyr Asn Gly Leu Ile Gly Leu Phe Leu Leu	
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gac ttt gta ctg aat gga ctt tta cgt aca gat aaa agc aaa agg tat Asp Phe Val Leu Asn Gly Leu Leu Arg Thr Asp Lys Ser Lys Arg Tyr 565 570 575	2014
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tat ctt att tct ggt ctg tca ttt att agt gtg att gcc tta atc atg Tyr Leu Ile Ser Gly Leu Ser Phe Ile Ser Val Ile Ala Leu Ile Met 630 635 640	2206
agc cat att ttt cat gcc aaa gct agt gtt gat tac tat tat ttg gta Ser His Ile Phe His Ala Lys Ala Ser Val Asp Tyr Tyr Tyr Leu Val 645 650 655	2254
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caa gaa caa atg tta tgg cag ttt cca ggt tta ttg ctg ggg gtt tgt	2878
Gln Glu Gln Met Leu Trp Gln Phe Pro Gly Leu Leu Leu Gly Val Cys	
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Phe Ile Leu Leu Ala Arg Thr Ile Asp Gln Lys Val Lys Asn Ala Phe	
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cca att gct att atc tgg att act ttg aca ttg ttt tat ctt aat tta	2974
Pro Ile Ala Ile Ile Trp Ile Thr Leu Thr Leu Phe Tyr Leu Asn Leu	
885 890 895	
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Gly His Ile Ser Trp Arg Leu Ser Phe Trp Phe Ile Leu Leu Leu Leu	
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915 920 925	
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Ser Trp Glu Glu Arg Ile Lys Asp Gly Ile Ile Ile Val Ser Leu Met	
930 935 940 945	
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965 970 975	
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Pro Ile Ala Leu Ala Thr Leu Ile Leu Thr Leu Val Tyr Leu Cys Leu	
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His Gln Trp Arg Met Leu Val Ile Phe Leu Val Ser Ser Met Ile Leu	
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Phe Tyr Ile Met Tyr Leu Glu Thr Leu Ala Thr Gln Ser Asn Met Thr	
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Gly Lys Ile Phe Ser Met Ser Lys Glu Glu Leu Ser Tyr Leu Pro Val
 35 40 45
 Ile Lys Leu Phe Lys Asn Gln Gly Val Tyr Asn Gly Leu Ile Gly Leu
 50 55 60
 Phe Leu Leu Tyr Gly Leu Tyr Ile Ser Gln Asn Gln Glu Ile Val Ala
 65 70 75 80
 Val Phe Leu Ile Asn Val Leu Leu Val Ala Ile Tyr Gly Ala Leu Thr
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 Val Asp Lys Lys Ile Leu Leu Lys Gln Gly Gly Leu Pro Ile Leu Ala
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 Leu Leu Thr Phe Leu Phe
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 35 40 45
 Tyr Gln Val Ile Val Met Asp Ser Arg Gly His Gly Lys Ser His Ala
 50 55 60
 Lys Leu Asn Thr Ile Ser Phe Arg Gln Ile Ala Val Asp Leu Lys Asp
 65 70 75 80
 Ile Leu Val His Leu Glu Ile Asp Lys Val Ile Leu Val Gly His Ser
 85 90 95
 Asp Gly Ala Asn Leu Ala Leu Val Phe Gln Thr Met Phe Pro Gly Met
 100 105 110
 Val Arg Gly Leu Leu Leu Asn Ser Gly Asn Leu Thr Ile His Gly Gln
 115 120 125
 Arg Trp Trp Asp Ile Leu Leu Val Arg Ile Ala Tyr Lys Phe Leu His
 130 135 140
 Tyr Leu Gly Lys Leu Phe Pro Tyr Met Arg Gln Lys Ala Gln Val Ile
 145 150 155 160
 Ser Leu Met Leu Glu Asp Leu Lys Ile Ser Pro Ala Asp Leu Gln His
 165 170 175
 Val Ser Thr Pro Val Met Val Leu Val Gly Asn Lys Asp Ile Ile Lys
 180 185 190
 Leu Asn His Ser Lys Lys Leu Ala Ser Tyr Phe Pro Arg Gly Glu Phe
 195 200 205
 Tyr Ser Leu Val Gly Phe Gly His His Ile Ile Lys Gln Asp Ser His
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 Glu Ile Val Glu Lys Ala Asn
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 Val Ile Ala Val Leu Pro Thr Thr Gly Tyr Asp Phe Val Leu Asn Gly
 35 40 45
 Leu Leu Arg Thr Asp Lys Ser Lys Arg Tyr Ile Leu Gln Thr Ser Trp
 50 55 60
 Cys Ile Asn Thr Phe Asn Asn Leu Ser Gly Phe Gly Gly Leu Ile Asp
 65 70 75 80
 Ile Gly Leu Arg Met Ala Phe Tyr Gly Lys Lys Gly Gln Glu Lys Ser
 85 90 95
 Asp Leu Arg Glu Val Thr Arg Phe Leu Pro Tyr Leu Ile Ser Gly Leu
 100 105 110
 Ser Phe Ile Ser Val Ile Ala Leu Ile Met Ser His Ile Phe His Ala
 115 120 125
 Lys Ala Ser Val Asp Tyr Tyr Leu Val Leu Ile Gly Ala Ser Met
 130 135 140
 Tyr Phe Pro Val Ile Tyr Trp Ile Ser Gly His Lys Gly Ser His Tyr
 145 150 155 160
 Phe Gly Asp Met Pro Ser Ser Thr Arg Ile Lys Leu Gly Val Val Ser
 165 170 175
 Phe Phe Glu Trp Gly Cys Ala Ala Ala Phe Ile Ile Ile Gly Tyr
 180 185 190
 Leu Met Gly Ile His Leu Pro Val Tyr Lys Ile Leu Pro Leu Phe Cys
 195 200 205
 Ile Gly Cys Ala Val Gly Ile Val Ser Leu Ile Pro Gly Gly Leu Gly
 210 215 220
 Ser Phe Glu Leu Val Leu Phe Thr Gly Phe Ala Ala Glu Gly Leu Pro
 225 230 235 240
 Lys Glu Thr Val Val Ala Trp Leu Leu Leu Tyr Arg Leu Ala Tyr Tyr
 245 250 255
 Ile Ile Pro Phe Phe Ala Gly Ile Tyr Phe Phe Ile His Tyr Leu Gly
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 Ser Gln Ile Asn Gln Arg Tyr Glu Asn Val Pro Lys Glu Leu Val Ser
 275 280 285
 Thr Val Leu Gln Thr Met Val Ser His Leu Met Arg Ile Leu Gly Ala
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 Phe Leu Ile Phe Ser Thr Ala Phe Phe Glu Asn Ile Thr Tyr Ile Met
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 Trp Leu Gln Lys Leu Gly Leu Asp Pro Leu Gln Glu Gln Met Leu Trp
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 Gln Phe Pro Gly Leu Leu Leu Gly Val Cys Phe Ile Leu Leu Ala Arg
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 Thr Ile Asp Gln Lys Val Lys Asn Ala Phe Pro Ile Ala Ile Ile Trp
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 Ile Thr Leu Thr Leu Phe Tyr Leu Asn Leu Gly His Ile Ser Trp Arg
 370 375 380
 Leu Ser Phe Trp Phe Ile Leu Leu Leu Gly Leu Leu Val Ile Lys
 385 390 395 400
 Pro Thr Leu Tyr Lys Lys Gln Phe Ile Tyr Ser Trp Glu Glu Arg Ile
 405 410 415
 Lys Asp Gly Ile Ile Ile Val Ser Leu Met Gly Val Leu Phe Tyr Ile
 420 425 430

Ala Gly Leu Leu Phe Pro Ile Arg Ala His Ile Thr Gly Gly Ser Ile
 435 440 445
 Glu Arg Leu His Tyr Ile Ile Ala Trp Glu Pro Ile Ala Leu Ala Thr
 450 455 460
 Leu Ile Leu Thr Leu Val Tyr Leu Cys Leu Val Lys Ile Leu Gln Gly
 465 470 475 480
 Lys Ser Cys Gln Ile Gly Asp Val Phe Asn Val Asp Arg Tyr Lys Lys
 485 490 495
 Leu Leu Gln Ala Tyr Gly Gly Ser Ser Asp Ser Gly Leu Ala Phe Leu
 500 505 510
 Asn Asp Lys Arg Leu Tyr Trp Tyr Gln Lys Asn Gly Glu Asp Cys Val
 515 520 525
 Ala Phe Gln Phe Val Ile Val Asn Asn Lys Cys Leu Ile Met Gly Glu
 530 535 540
 Pro Ala Gly Asp Asp Thr Tyr Ile Arg Glu Ala Ile Glu Ser Phe Ile
 545 550 555 560
 Asp Asp Ala Asp Lys Leu Asp Tyr Asp Leu Val Phe Tyr Ser Ile Gly
 565 570 575
 Gln Lys Leu Thr Leu Leu His Glu Tyr Gly Phe Asp Phe Met Lys
 580 585 590
 Val Gly Glu Asp Ala Leu Val Asn Leu Glu Thr Phe Thr Leu Lys Gly
 595 600 605
 Asn Lys Tyr Lys Pro Phe Arg Asn Ala Leu Asn Arg Val Glu Lys Asp
 610 615 620
 Gly Phe Tyr Phe Glu Val Val Gln Ser Pro His Ser Gln Glu Leu Leu
 625 630 635 640
 Asn Ser Leu Glu Glu Ile Ser Asn Thr Trp Leu Glu Gly Arg Pro Glu
 645 650 655
 Lys Gly Phe Ser Leu Gly Tyr Phe Asn Lys Asp Tyr Phe Gln Gln Ala
 660 665 670
 Pro Ile Ala Leu Val Lys Asn Ala Glu His Glu Val Val Ala Phe Ala
 675 680 685
 Asn Ile Met Pro Asn Tyr Glu Lys Ser Ile Ile Ser Ile Asp Leu Met
 690 695 700
 Arg His Asp Lys Gln Lys Ile Pro Asn Gly Val Met Asp Phe Leu Phe
 705 710 715 720
 Leu Ser Leu Phe Ser Tyr Tyr Gln Glu Lys Gly Tyr His Tyr Phe Asp
 725 730 735
 Leu Gly Met Ala Pro Leu Ser Gly Val Gly Arg Val Glu Thr Ser Phe
 740 745 750
 Ala Lys Glu Arg Met Ala Tyr Leu Val Tyr His Phe Gly Ser His Phe
 755 760 765
 Tyr Ser Phe Asn Gly Leu His Lys Tyr Lys Lys Phe Thr Pro Leu
 770 775 780
 Trp Ser Glu Arg Tyr Ile Ser Cys Ser Arg Ser Ser Trp Leu Ile Cys
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 805 810 815

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 Gln Glu Gln Met Leu Trp Gln Phe Pro Gly Leu Leu Leu Gly Val Cys
 35 40 45
 Phe Ile Leu Leu Ala Arg Thr Ile Asp Gln Lys Val Lys Asn Ala Phe
 50 55 60
 Pro Ile Ala Ile Ile Trp Ile Thr Leu Thr Leu Phe Tyr Leu Asn Leu
 65 70 75 80
 Gly His Ile Ser Trp Arg Leu Ser Phe Trp Phe Ile Leu Leu Leu
 85 90 95
 Gly Leu Leu Val Ile Lys Pro Thr Leu Tyr Lys Lys Gln Phe Ile Tyr
 100 105 110
 Ser Trp Glu Glu Arg Ile Lys Asp Gly Ile Ile Val Ser Leu Met
 115 120 125
 Gly Val Leu Phe Tyr Ile Ala Gly Leu Leu Phe Pro Ile Arg Ala His
 130 135 140
 Ile Thr Gly Gly Ser Ile Glu Arg Leu His Tyr Ile Ile Ala Trp Glu
 145 150 155 160
 Pro Ile Ala Leu Ala Thr Leu Ile Leu Thr Leu Val Tyr Leu Cys Leu
 165 170 175
 Val Lys Ile Leu Gln Gly Lys Ser Cys Gln Ile Gly Asp Val Phe Asn
 180 185 190
 Val Asp Arg Tyr Lys Lys Leu Leu Gln Ala Tyr Gly Gly Ser Ser Asp
 195 200 205
 Ser Gly Leu Ala Phe Leu Asn Asp Lys Arg Leu Tyr Trp Tyr Gln Lys
 210 215 220
 Asn Gly Glu Asp Cys Val Ala Phe Gln Phe Val Ile Val Asn Asn Lys
 225 230 235 240
 Cys Leu Ile Met Gly Glu Pro Ala Gly Asp Asp Thr Tyr Ile Arg Glu
 245 250 255
 Ala Ile Glu Ser Phe Ile Asp Asp Ala Asp Lys Leu Asp Tyr Asp Leu
 260 265 270
 Val Phe Tyr Ser Ile Gly Gln Lys Leu Thr Leu Leu Leu His Glu Tyr
 275 280 285
 Gly Phe Asp Phe Met Lys Val Gly Glu Asp Ala Leu Val Asn Leu Glu
 290 295 300
 Thr Phe Thr Leu Lys Gly Asn Lys Tyr Lys Pro Phe Arg Asn Ala Leu
 305 310 315 320
 Asn Arg Val Glu Lys Asp Gly Phe Tyr Phe Glu Val Val Gln Ser Pro
 325 330 335
 His Ser Gln Glu Leu Leu Asn Ser Leu Glu Ile Ser Asn Thr Trp
 340 345 350
 Leu Glu Gly Arg Pro Glu Lys Gly Phe Ser Leu Gly Tyr Phe Asn Lys
 355 360 365
 Asp Tyr Phe Gln Gln Ala Pro Ile Ala Leu Val Lys Asn Ala Glu His
 370 375 380
 Glu Val Val Ala Phe Ala Asn Ile Met Pro Asn Tyr Glu Lys Ser Ile
 385 390 395 400
 Ile Ser Ile Asp Leu Met Arg His Asp Lys Gln Lys Ile Pro Asn Gly
 405 410 415
 Val Met Asp Phe Leu Phe Leu Ser Leu Phe Ser Tyr Tyr Gln Glu Lys
 420 425 430
 Gly Tyr His Tyr Phe Asp Leu Gly Met Ala Pro Leu Ser Gly Val Gly
 435 440 445

Arg Val Glu Thr Ser Phe Ala Lys Glu Arg Met Ala Tyr Leu Val Tyr
 450 455 460
 His Phe Gly Ser His Phe Tyr Ser Phe Asn Gly Leu His Lys Tyr Lys
 465 470 475 480
 Lys Lys Phe Thr Pro Leu Trp Ser Glu Arg Tyr Ile Ser Cys Ser Arg
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 Lys Ile Lys Ile Val Lys
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 Ser Leu Leu Glu Lys Ile Ser Val Glu Arg Ser Phe Ile Glu Phe Asp
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aaa ctt cta tta gca cct tat tgg cgt aaa gga atg ctg gca cta ata 144
 Lys Leu Leu Ala Pro Tyr Trp Arg Lys Gly Met Leu Ala Leu Ile
 35 40 45

gat agt cat gct ttt aat tat cta cca tgc tta aaa aat agg gaa tta 192
 Asp Ser His Ala Phe Asn Tyr Leu Pro Cys Leu Lys Asn Arg Glu Leu
 50 55 60

caa tta agc gcc ttt ttg tcc cag tta gat aaa gat ttt tta ttt gag 240
 Gln Leu Ser Ala Phe Leu Ser Gln Leu Asp Lys Asp Phe Leu Phe Glu
 65 70 75 80

aca tca gaa caa gct tgg gca tca ctc atc ttg agt atg gaa gtt gaa 288
 Thr Ser Glu Gln Ala Trp Ala Ser Leu Ile Leu Ser Met Glu Val Glu
 85 90 95

cac aca aag act ttt tta aaa aaa tgg aag aca tca act cac ttt caa	336
His Thr Lys Thr Phe Leu Lys Lys Trp Lys Thr Ser Thr His Phe Gln	
100 105 110	
aaa gat gtt gag cat ata gtg gat gtt tat cgt att cgt gaa caa atg	384
Lys Asp Val Glu His Ile Val Asp Val Tyr Arg Ile Arg Glu Gln Met	
115 120 125	
gga ttg gct aaa gaa cat ctt tat cgt tat gga aaa act ata ata aaa	432
Gly Leu Ala Lys Glu His Leu Tyr Arg Tyr Gly Lys Thr Ile Ile Lys	
130 135 140	
caa gcg gaa ggt att cgc aaa gca aga ggc ttg atg gtt gat ttc gaa	480
Gln Ala Glu Gly Ile Arg Lys Ala Arg Gly Leu Met Val Asp Phe Glu	
145 150 155 160	
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Lys Ile Glu Gln Leu Asp Ser Glu Leu Ala Ile His Asp Arg His Glu	
165 170 175	
ata gtt gtc aat ggt ggc acc tta atc aag aaa tta gga ata aaa cct	576
Ile Val Val Asn Gly Gly Thr Leu Ile Lys Lys Leu Gly Ile Lys Pro	
180 185 190	
ggt cca cag atg gga gat att atc tct caa att gaa tta gcc att gtt	624
Gly Pro Gln Met Gly Asp Ile Ile Ser Gln Ile Glu Leu Ala Ile Val	
195 200 205	
tta gga caa ctg att aat gaa gaa gag gct att tta cat ttt gtt aag	672
Leu Gly Gln Leu Ile Asn Glu Glu Ala Ile Leu His Phe Val Lys	
210 215 220	
cag tac ttg atg gat tagagaggat tat atg agc gat ttt tta gta gat	721
Gln Tyr Leu Met Asp Met Ser Asp Phe Leu Val Asp	
225 230 235	
gga ttg act aag tcg gtt ggt gat aag acg gtc ttt agt aat gtt tca	769
Gly Leu Thr Lys Ser Val Gly Asp Lys Thr Val Phe Ser Asn Val Ser	
240 245 250	
ttt atc atc cat agt tta gac cgt att ggg att att ggt gtc aat gga	817
Phe Ile Ile His Ser Leu Asp Arg Ile Gly Ile Ile Gly Val Asn Gly	
255 260 265	
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Thr Gly Lys Thr Thr Leu Leu Asp Val Ile Ser Gly Glu Leu Gly Phe	
270 275 280	
gat ggt gat cgt tcc cct ttt tca tca gct aat gat tat aag att gct	913
Asp Gly Asp Arg Ser Pro Phe Ser Ser Ala Asn Asp Tyr Lys Ile Ala	
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tat tta aaa caa gaa cca gac ttt gat gat tct cag aca att ttg gac	961
Tyr Leu Lys Gln Glu Pro Asp Phe Asp Asp Ser Gln Thr Ile Leu Asp	
305 310 315	

acc gta ctt tct tct gac tta aga gag atg gct tta att aaa gaa tat	1009
Thr Val Leu Ser Ser Asp Leu Arg Glu Met Ala Leu Ile Lys Glu Tyr	
320 325 330	
gaa tta ttg ctt aat cac tac gaa gaa agt aag caa tca cgt cta gag	1057
Glu Leu Leu Asn His Tyr Glu Glu Ser Lys Gln Ser Arg Leu Glu	
335 340 345	
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Lys Val Met Ala Glu Met Asp Ser Leu Asp Ala Trp Ser Ile Glu Ser	
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gaa gtc aaa aca gta tta tcc aaa tta ggt att act gat ttg cag ttg	1153
Glu Val Lys Thr Val Leu Ser Lys Leu Gly Ile Thr Asp Leu Gln Leu	
365 370 375 380	
tcg gtt ggt gaa tta tca gga gga tta cga aga cgt gtt caa tta gcg	1201
Ser Val Gly Glu Leu Ser Gly Gly Leu Arg Arg Val Gln Leu Ala	
385 390 395	
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Gln Val Leu Leu Asn Asp Ala Asp Leu Leu Leu Asp Glu Pro Thr	
400 405 410	
aac cac tta gat att gac act att gca tgg tta acg aat ttt ttg aaa	1297
Asn His Leu Asp Ile Asp Thr Ile Ala Trp Leu Thr Asn Phe Leu Lys	
415 420 425	
aat agt aaa aag aca gtg ctt ttt ata act cat gat cgt tat ttt cta	1345
Asn Ser Lys Lys Thr Val Leu Phe Ile Thr His Asp Arg Tyr Phe Leu	
430 435 440	
gac aat gtt gca aca cgt att ttt gaa tta gat aag gca cag att aca	1393
Asp Asn Val Ala Thr Arg Ile Phe Glu Leu Asp Lys Ala Gln Ile Thr	
445 450 455 460	
gaa tat caa ggc aat tat cag gat tat gtc cga ctt cgt gca gaa caa	1441
Glu Tyr Gln Gly Asn Tyr Gln Asp Tyr Val Arg Leu Arg Ala Glu Gln	
465 470 475	
gac gag cgt gat gct gct agt tta cat aaa aag aaa cag ctt tat aaa	1489
Asp Glu Arg Asp Ala Ala Ser Leu His Lys Lys Lys Gln Leu Tyr Lys	
480 485 490	
cag gaa cta gct tgg atg cgt act cag cca caa gct cgt gca acg aaa	1537
Gln Glu Leu Ala Trp Met Arg Thr Gln Pro Gln Ala Arg Ala Thr Lys	
495 500 505	
caa cag gct cgt att aat cgt ttt caa aat cta aaa aac gat tta cac	1585
Gln Gln Ala Arg Ile Asn Arg Phe Gln Asn Leu Lys Asn Asp Leu His	
510 515 520	
caa aca agc gat aca agc gat ttg gaa atg aca ttt gaa aca agt cga	1633
Gln Thr Ser Asp Thr Ser Asp Leu Glu Met Thr Phe Glu Thr Ser Arg	
525 530 535 540	

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545 550 555	
gat aaa tct atc ttg aaa gac ttt aat ttg tta att caa aat aaa gac Asp Lys Ser Ile Leu Lys Asp Phe Asn Leu Leu Ile Gln Asn Lys Asp	1729
560 565 570	
cgt att ggc atc gtt gga gat aat ggt gtt gga aag tca acc tta ctt Arg Ile Gly Ile Val Gly Asp Asn Gly Val Gly Lys Ser Thr Leu Leu	1777
575 580 585	
aat tta att gtt caa gat tta cag ccg gat tcg ggt aat gtc tct att Asn Leu Ile Val Gln Asp Leu Gln Pro Asp Ser Gly Asn Val Ser Ile	1825
590 595 600	
ggt gaa acg ata cgt gta ggt tac ttt tca caa caa ctt cat aat atg Gly Glu Thr Ile Arg Val Gly Tyr Phe Ser Gln Gln Leu His Asn Met	1873
605 610 615 620	
gat ggc tca aaa cgt gtt att aat tat ttg caa gag gtt gca gat gag Asp Gly Ser Lys Arg Val Ile Asn Tyr Leu Gln Glu Val Ala Asp Glu	1921
625 630 635	
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640 645 650	
ttt ctc ttt cca cgt tcg aca cat gga aca caa att gca aaa tta tca Phe Leu Phe Pro Arg Ser Thr His Gly Thr Gln Ile Ala Lys Leu Ser	2017
655 660 665	
ggt ggt gag aaa aaa aga ctt tac ctt tta aaa atc ctg att gaa aag Gly Gly Glu Lys Lys Arg Leu Tyr Leu Leu Lys Ile Leu Ile Glu Lys	2065
670 675 680	
cct aat gtg tta cta ctt gat gag ccg aca aat gac tta gat att gct Pro Asn Val Leu Leu Asp Glu Pro Thr Asn Asp Leu Asp Ile Ala	2113
685 690 695 700	
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705 710 715	
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720 725 730	
att att gcg ttt gaa gat aac gat atc cgt gaa ttt ttt ggt aat tat Ile Ile Ala Phe Glu Asp Asn Asp Ile Arg Glu Phe Phe Gly Asn Tyr	2257
735 740 745	
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750 755 760	

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gat att atg ata ttg gaa aat act atc act cgt ata gaa aat gat atg Asp Ile Met Ile Leu Glu Asn Thr Ile Thr Arg Ile Glu Asn Asp Met 800 805 810	2449
caa aca tgt ggt agt gat ttt aca agg tta tct gat tta caa aag gaa Gln Thr Cys Gly Ser Asp Phe Thr Arg Leu Ser Asp Leu Gln Lys Glu 815 820 825	2497
tta gat gca aaa aat gaa gca ctt cta gaa aag tat gac cgt tat gag Leu Asp Ala Lys Asn Glu Ala Leu Leu Glu Lys Tyr Asp Arg Tyr Glu 830 835 840	2545
tac ctt agt gag ttagacac atg att atc cgt ccg att att aaa aat gat Tyr Leu Ser Glu LeuAspThrMet Ile Ile Arg Pro Ile Ile Lys Asn Asp 845 850 855 860	2595
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acc tca tac tac gaa aaa ata gag aag tca gga ttc ttt gtc att gag Thr Ser Tyr Tyr Glu Lys Ile Glu Lys Ser Gly Phe Phe Val Ile Glu 895 900 905	2739
gag aga gat gag att att ggc tgt ggc ggc ttt ggt ccg ctg aaa aat Glu Arg Asp Glu Ile Ile Gly Cys Gly Gly Phe Gly Pro Leu Lys Asn 910 915 920 925	2787
cta att gca gag atg cag aag gtg tac att gca gaa cgt ttc cgt ggt Leu Ile Ala Glu Met Gln Lys Val Tyr Ile Ala Glu Arg Phe Arg Gly 930 935 940	2835
aag ggg ctt gct act gat tta gtg aaa atg att gaa gta gaa gct cga Lys Gly Leu Ala Thr Asp Leu Val Lys Met Ile Glu Val Glu Ala Arg 945 950 955	2883
aaa att ggg tat aga caa ctt tat tta gag aca gcc agt act ttg agt Lys Ile Gly Tyr Arg Gln Leu Tyr Leu Glu Thr Ala Ser Thr Leu Ser 960 965 970	2931
agg gca act gcg gtt tat aag cat atg gga tat tgt gcc tta tcg caa Arg Ala Thr Ala Val Tyr Lys His Met Gly Tyr Cys Ala Leu Ser Gln 975 980 985	2979

cca ata gca aat gat caa ggt cat aca gct atg gat att tgg atg att Pro Ile Ala Asn Asp Gln Gly His Thr Ala Met Asp Ile Trp Met Ile 990 995 1000 1005	3027
aaa gat tta taagttgaaa gtggattagt gaacatggat taattatTTT Lys Asp Leu	3076
gagataagag gaaagaaaaag gagacatat atg gca tat att tgg tct tat ttg Met Ala Tyr Ile Trp Ser Tyr Leu 1010 1015	3129
aaa agg tac ccc aat tgg tta tgg ctt gat tta cta gga gct atg ctt Lys Arg Tyr Pro Asn Trp Leu Trp Leu Asp Leu Leu Gly Ala Met Leu 1020 1025 1030	3177
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gat aat ggc gtt aca aaa ggt gat cgg act gga gtt tat ctg tgg acg Asp Asn Gly Val Thr Lys Gly Asp Arg Thr Gly Val Tyr Leu Trp Thr 1050 1055 1060	3273
ttc atc atg ttt ata ttt gtt gta cta ggt att att ggg cgt att acg Phe Ile Met Phe Ile Phe Val Val Leu Gly Ile Ile Gly Arg Ile Thr 1065 1070 1075 1080	3321
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cgt aat gat atg tat gct aag ctt caa gaa tac tcc cat cat gaa tat Arg Asn Asp Met Tyr Ala Lys Leu Gln Glu Tyr Ser His His Glu Tyr 1100 1105 1110	3417
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cca tct ttg gct tgg ctt gta gcg gtt gcg atg cct ctt ttg gta gga Pro Ser Leu Ala Trp Leu Val Ala Val Ala Met Pro Leu Leu Val Gly 1165 1170 1175	3609
gtc gtt tta tat gta gct ata aaa aca aaa cct tta tct gaa aga caa Val Val Leu Tyr Val Ala Ile Lys Thr Lys Pro Leu Ser Glu Arg Gln 1180 1185 1190	3657

cag act atg ctt gat aaa atc aat caa tat gtt cgt gaa aat tta aca	3705
Gln Thr Met Leu Asp Lys Ile Asn Gln Tyr Val Arg Glu Asn Leu Thr	
1195 1200 1205	
ggg tta cgc gtt gtt aga gcc ttt gca aga gag aat ttt caa tca caa	3753
Gly Leu Arg Val Val Arg Ala Phe Ala Arg Glu Asn Phe Gln Ser Gln	
1210 1215 1220	
aaa ttt caa gtc gct aac caa cgt tac aca gat act tca act ggt ctt	3801
Lys Phe Gln Val Ala Asn Gln Arg Tyr Thr Asp Thr Ser Thr Gly Leu	
1225 1230 1235 1240	
ttt aaa tta aca ggg cta aca gaa cca ctt ttc gtt caa att att att	3849
Phe Lys Leu Thr Gly Leu Thr Glu Pro Leu Phe Val Gln Ile Ile Ile	
1245 1250 1255	
gca atg att gtg gct atc gtt tgg ttt gct ttg gat ccc tta caa aga	3897
Ala Met Ile Val Ala Ile Val Trp Phe Ala Leu Asp Pro Leu Gln Arg	
1260 1265 1270	
ggt gct att aaa ata ggg gat tta gtt gct ttt atc gaa tat agc ttc	3945
Gly Ala Ile Lys Ile Gly Asp Leu Val Ala Phe Ile Glu Tyr Ser Phe	
1275 1280 1285	
cat gct ctc ttt tca ttt ttg cta ttt gcc aat ctt ttt act atg tat	3993
His Ala Leu Phe Ser Phe Leu Leu Phe Ala Asn Leu Phe Thr Met Tyr	
1290 1295 1300	
cct cgt atg gtg gta tca agc cat cgt att aga gag gtg atg gat atg	4041
Pro Arg Met Val Val Ser Ser His Arg Ile Arg Glu Val Met Asp Met	
1305 1310 1315 1320	
cca atc tct atc aat cct aat gcc gaa ggt gtt acg gat acg aaa ctt	4089
Pro Ile Ser Ile Asn Pro Asn Ala Glu Gly Val Thr Asp Thr Lys Leu	
1325 1330 1335	
aaa ggg cat tta gaa ttt gat aat gta aca ttc gct tat cca gga gaa	4137
Lys Gly His Leu Glu Phe Asp Asn Val Thr Phe Ala Tyr Pro Gly Glu	
1340 1345 1350	
aca gag agt ccc gtt ttg cat gat att tct ttt aaa gct aag cct gga	4185
Thr Glu Ser Pro Val Leu His Asp Ile Ser Phe Lys Ala Lys Pro Gly	
1355 1360 1365	
gaa aca att gct ttt att ggt tca aca ggt tca gga aaa tct tct ctt	4233
Glu Thr Ile Ala Phe Ile Gly Ser Thr Gly Ser Gly Lys Ser Ser Leu	
1370 1375 1380	
gtt aat ttg att cca cgt ttt tat gat gtg aca ctt gga aaa atc tta	4281
Val Asn Leu Ile Pro Arg Phe Tyr Asp Val Thr Leu Gly Lys Ile Leu	
1385 1390 1395 1400	
gta gat gga gtt gat gta aga gat tat aac ctt aaa tca ctt cgc caa	4329
Val Asp Gly Val Asp Val Arg Asp Tyr Asn Leu Lys Ser Leu Arg Gln	
1405 1410 1415	

aag att gga ttt atc ccc caa aaa gct ctt tta ttt aca ggg aca ata Lys Ile Gly Phe Ile Pro Gln Lys Ala Leu Leu Phe Thr Gly Thr Ile 1420 1425 1430	4377
gga gag aat tta aaa tat gga aaa gct gat gct act att gat gat ctt Gly Glu Asn Leu Lys Tyr Gly Lys Ala Asp Ala Thr Ile Asp Asp Leu 1435 1440 1445	4425
aga caa gcg gtt gat att tct caa gct aaa gag ttt att gag agt cac Arg Gln Ala Val Asp Ile Ser Gln Ala Lys Glu Phe Ile Glu Ser His 1450 1455 1460	4473
caa gaa gcc ttt gaa acg cat tta gct gaa ggt ggg agc aat ctt tct Gln Glu Ala Phe Glu Thr His Leu Ala Glu Gly Ser Asn Leu Ser 1465 1470 1475 1480	4521
ggg ggt caa aaa caa cgg tta tct att gct agg gct gtt gtt aaa gat Gly Gly Gln Lys Gln Arg Leu Ser Ile Ala Arg Ala Val Val Lys Asp 1485 1490 1495	4569
cca gat tta tat att ttt gat gat tca ttt tct gct ctc gat tat aag Pro Asp Leu Tyr Ile Phe Asp Asp Ser Phe Ser Ala Leu Asp Tyr Lys 1500 1505 1510	4617
aca gac gct act tta aga gcg cgt cta aaa gaa gta acc ggt gat tct Thr Asp Ala Thr Leu Arg Ala Arg Leu Lys Glu Val Thr Gly Asp Ser 1515 1520 1525	4665
aca gtt ttg ata gtt gct caa agg gtg ggt acg att atg gat gct gat Thr Val Leu Ile Val Ala Gln Arg Val Gly Thr Ile Met Asp Ala Asp 1530 1535 1540	4713
cag att att gtc ctt gat gaa ggc gaa att gtc ggt cgt ggt acc cac Gln Ile Ile Val Leu Asp Glu Gly Glu Ile Val Gly Arg Gly Thr His 1545 1550 1555 1560	4761
gct caa tta ata gaa aat aat gct att tat cgt gaa atc gct gag tca Ala Gln Leu Ile Glu Asn Asn Ala Ile Tyr Arg Glu Ile Ala Glu Ser 1565 1570 1575	4809
caa ctg aag aac caa aac tta tca gaa gga gag tgattgt atg aga aaa Gln Leu Lys Asn Gln Asn Leu Ser Glu Gly Glu Met Arg Lys 1580 1585 1590	4858
aaa tct gtt ttt ttg aga tta tgg tct tac cta act cgc tac aaa gct Lys Ser Val Phe Leu Arg Leu Trp Ser Tyr Leu Thr Arg Tyr Lys Ala 1595 1600 1605	4906
act ctt ttc tta gcg att ttt ttg aaa gtt tta tct agt ttt atg agt Thr Leu Phe Leu Ala Ile Phe Leu Lys Val Leu Ser Ser Phe Met Ser 1610 1615 1620	4954
gtt ctg gag cct ttt att tta ggg tta gcg ata aca gag ttg act gct Val Leu Glu Pro Phe Ile Leu Gly Leu Ala Ile Thr Glu Leu Thr Ala 1625 1630 1635	5002

aac ctt gtt gat atg gct aag gga gtt tct ggg gca gaa ttg aac gtt 5050
 Asn Leu Val Asp Met Ala Lys Gly Val Ser Gly Ala Glu Leu Asn Val
 1640 1645 1650

cct tat att gct ggt att ttg att att tat ttt ttc aga ggt gtt ttc 5098
 Pro Tyr Ile Ala Gly Ile Leu Ile Tyr Phe Phe Arg Gly Val Phe
 1655 1660 1665 1670

tat gaa tta ggt tct tat ggc tca aat t 5126
 Tyr Glu Leu Gly Ser Tyr Gly Ser Asn
 1675

<210> 8
 <211> 229
 <212> PRT
 <213> Streptococcus

<400> 8
 Asn Phe Asp Ile Glu Thr Thr Phe Glu Ala Met Lys Lys His Ala
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 Ser Leu Leu Glu Lys Ile Ser Val Glu Arg Ser Phe Ile Glu Phe Asp
 20 25 30
 Lys Leu Leu Ala Pro Tyr Trp Arg Lys Gly Met Leu Ala Leu Ile
 35 40 45
 Asp Ser His Ala Phe Asn Tyr Leu Pro Cys Leu Lys Asn Arg Glu Leu
 50 55 60
 Gln Leu Ser Ala Phe Leu Ser Gln Leu Asp Lys Asp Phe Leu Phe Glu
 65 70 75 80
 Thr Ser Glu Gln Ala Trp Ala Ser Leu Ile Leu Ser Met Glu Val Glu
 85 90 95
 His Thr Lys Thr Phe Leu Lys Trp Lys Thr Ser Thr His Phe Gln
 100 105 110
 Lys Asp Val Glu His Ile Val Asp Val Tyr Arg Ile Arg Glu Gln Met
 115 120 125
 Gly Leu Ala Lys Glu His Leu Tyr Arg Tyr Gly Lys Thr Ile Ile Lys
 130 135 140
 Gln Ala Glu Gly Ile Arg Lys Ala Arg Gly Leu Met Val Asp Phe Glu
 145 150 155 160
 Lys Ile Glu Gln Leu Asp Ser Glu Leu Ala Ile His Asp Arg His Glu
 165 170 175
 Ile Val Val Asn Gly Gly Thr Leu Ile Lys Lys Leu Gly Ile Lys Pro
 180 185 190
 Gly Pro Gln Met Gly Asp Ile Ile Ser Gln Ile Glu Leu Ala Ile Val
 195 200 205
 Leu Gly Gln Leu Ile Asn Glu Glu Ala Ile Leu His Phe Val Lys
 210 215 220
 Gln Tyr Leu Met Asp
 225

<210> 9
 <211> 622
 <212> PRT
 <213> Streptococcus

<400> 9
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 1 5 10 15
 Thr Val Phe Ser Asn Val Ser Phe Ile Ile His Ser Leu Asp Arg Ile
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 Gly Ile Ile Gly Val Asn Gly Thr Gly Lys Thr Thr Leu Leu Asp Val
 35 40 45
 Ile Ser Gly Glu Leu Gly Phe Asp Gly Asp Arg Ser Pro Phe Ser Ser
 50 55 60
 Ala Asn Asp Tyr Lys Ile Ala Tyr Leu Lys Gln Glu Pro Asp Phe Asp
 65 70 75 80
 Asp Ser Gln Thr Ile Leu Asp Thr Val Leu Ser Ser Asp Leu Arg Glu
 85 90 95
 Met Ala Leu Ile Lys Glu Tyr Glu Leu Leu Asn His Tyr Glu Glu
 100 105 110
 Ser Lys Gln Ser Arg Leu Glu Lys Val Met Ala Glu Met Asp Ser Leu
 115 120 125
 Asp Ala Trp Ser Ile Glu Ser Glu Val Lys Thr Val Leu Ser Lys Leu
 130 135 140
 Gly Ile Thr Asp Leu Gln Leu Ser Val Gly Glu Leu Ser Gly Gly Leu
 145 150 155 160
 Arg Arg Arg Val Gln Leu Ala Gln Val Leu Leu Asn Asp Ala Asp Leu
 165 170 175
 Leu Leu Leu Asp Glu Pro Thr Asn His Leu Asp Ile Asp Thr Ile Ala
 180 185 190
 Trp Leu Thr Asn Phe Leu Lys Asn Ser Lys Lys Thr Val Leu Phe Ile
 195 200 205
 Thr His Asp Arg Tyr Phe Leu Asp Asn Val Ala Thr Arg Ile Phe Glu
 210 215 220
 Leu Asp Lys Ala Gln Ile Thr Glu Tyr Gln Gly Asn Tyr Gln Asp Tyr
 225 230 235 240
 Val Arg Leu Arg Ala Glu Gln Asp Glu Arg Asp Ala Ala Ser Leu His
 245 250 255
 Lys Lys Lys Gln Leu Tyr Lys Gln Glu Leu Ala Trp Met Arg Thr Gln
 260 265 270
 Pro Gln Ala Arg Ala Thr Lys Gln Gln Ala Arg Ile Asn Arg Phe Gln
 275 280 285
 Asn Leu Lys Asn Asp Leu His Gln Thr Ser Asp Thr Ser Asp Leu Glu
 290 295 300
 Met Thr Phe Glu Thr Ser Arg Ile Gly Lys Lys Val Ile Asn Phe Glu
 305 310 315 320
 Asn Val Ser Phe Ser Tyr Pro Asp Lys Ser Ile Leu Lys Asp Phe Asn
 325 330 335
 Leu Leu Ile Gln Asn Lys Asp Arg Ile Gly Ile Val Gly Asp Asn Gly
 340 345 350
 Val Gly Lys Ser Thr Leu Leu Asn Leu Ile Val Gln Asp Leu Gln Pro
 355 360 365
 Asp Ser Gly Asn Val Ser Ile Gly Glu Thr Ile Arg Val Gly Tyr Phe
 370 375 380
 Ser Gln Gln Leu His Asn Met Asp Gly Ser Lys Arg Val Ile Asn Tyr
 385 390 395 400
 Leu Gln Glu Val Ala Asp Glu Val Lys Thr Ser Val Gly Thr Thr Ser
 405 410 415
 Val Thr Glu Leu Leu Glu Gln Phe Leu Phe Pro Arg Ser Thr His Gly
 420 425 430

Thr Gln Ile Ala Lys Leu Ser Gly Gly Glu Lys Lys Arg Leu Tyr Leu
 435 440 445
 Leu Lys Ile Leu Ile Glu Lys Pro Asn Val Leu Leu Asp Glu Pro
 450 455 460
 Thr Asn Asp Leu Asp Ile Ala Thr Leu Thr Val Leu Glu Asn Phe Leu
 465 470 475 480
 Gln Gly Phe Gly Gly Pro Val Ile Thr Val Ser His Asp Arg Tyr Phe
 485 490 495
 Leu Asp Lys Val Ala Asn Lys Ile Ile Ala Phe Glu Asp Asn Asp Ile
 500 505 510
 Arg Glu Phe Phe Gly Asn Tyr Thr Asp Tyr Leu Asp Glu Lys Ala Phe
 515 520 525
 Asn Glu Gln Asn Asn Glu Val Ile Ser Lys Lys Glu Ser Thr Lys Thr
 530 535 540
 Ser Arg Glu Lys Gln Ser Arg Lys Arg Met Ser Tyr Phe Glu Lys Gln
 545 550 555 560
 Glu Trp Ala Thr Ile Glu Asp Asp Ile Met Ile Leu Glu Asn Thr Ile
 565 570 575
 Thr Arg Ile Glu Asn Asp Met Gln Thr Cys Gly Ser Asp Phe Thr Arg
 580 585 590
 Leu Ser Asp Leu Gln Lys Glu Leu Asp Ala Lys Asn Glu Ala Leu Leu
 595 600 605
 Glu Lys Tyr Asp Arg Tyr Glu Tyr Leu Ser Glu Leu Asp Thr
 610 615 620

<210> 10
 <211> 157
 <212> PRT
 <213> Streptococcus

<400> 10

Met Ile Ile Arg Pro Ile Ile Lys Asn Asp Asp Gln Ala Val Ala Gln
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 Ala Tyr Ser Asp Pro His Leu Asp His Leu Thr Ser Tyr Tyr Glu Lys
 35 40 45
 Ile Glu Lys Ser Gly Phe Phe Val Ile Glu Glu Arg Asp Glu Ile Ile
 50 55 60
 Gly Cys Gly Gly Phe Gly Pro Leu Lys Asn Leu Ile Ala Glu Met Gln
 65 70 75 80
 Lys Val Tyr Ile Ala Glu Arg Phe Arg Gly Lys Gly Leu Ala Thr Asp
 85 90 95
 Leu Val Lys Met Ile Glu Val Glu Ala Arg Lys Ile Gly Tyr Arg Gln
 100 105 110
 Leu Tyr Leu Glu Thr Ala Ser Thr Leu Ser Arg Ala Thr Ala Val Tyr
 115 120 125
 Lys His Met Gly Tyr Cys Ala Leu Ser Gln Pro Ile Ala Asn Asp Gln
 130 135 140
 Gly His Thr Ala Met Asp Ile Trp Met Ile Lys Asp Leu
 145 150 155

<210> 11
 <211> 579
 <212> PRT
 <213> Streptococcus

<400> 11
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 20 25 30
 Pro Thr Ala Leu Ala Gly Met Ile Asp Asn Gly Val Thr Lys Gly Asp
 35 40 45
 Arg Thr Gly Val Tyr Leu Trp Thr Phe Ile Met Phe Ile Phe Val Val
 50 55 60
 Leu Gly Ile Ile Gly Arg Ile Thr Met Ala Tyr Ala Ser Ser Arg Leu
 65 70 75 80
 Thr Thr Thr Met Ile Arg Asp Met Arg Asn Asp Met Tyr Ala Lys Leu
 85 90 95
 Gln Glu Tyr Ser His His Glu Tyr Glu Gln Ile Gly Val Ser Ser Leu
 100 105 110
 Val Thr Arg Met Thr Ser Asp Thr Phe Val Leu Met Gln Phe Ala Glu
 115 120 125
 Met Ser Leu Arg Leu Gly Leu Val Thr Pro Met Val Met Ile Phe Ser
 130 135 140
 Val Val Met Ile Leu Ile Thr Ser Pro Ser Leu Ala Trp Leu Val Ala
 145 150 155 160
 Val Ala Met Pro Leu Leu Val Gly Val Val Leu Tyr Val Ala Ile Lys
 165 170 175
 Thr Lys Pro Leu Ser Glu Arg Gln Gln Thr Met Leu Asp Lys Ile Asn
 180 185 190
 Gln Tyr Val Arg Glu Asn Leu Thr Gly Leu Arg Val Val Arg Ala Phe
 195 200 205
 Ala Arg Glu Asn Phe Gln Ser Gln Lys Phe Gln Val Ala Asn Gln Arg
 210 215 220
 Tyr Thr Asp Thr Ser Thr Gly Leu Phe Lys Leu Thr Gly Leu Thr Glu
 225 230 235 240
 Pro Leu Phe Val Gln Ile Ile Ala Met Ile Val Ala Ile Val Trp
 245 250 255
 Phe Ala Leu Asp Pro Leu Gln Arg Gly Ala Ile Lys Ile Gly Asp Leu
 260 265 270
 Val Ala Phe Ile Glu Tyr Ser Phe His Ala Leu Phe Ser Phe Leu Leu
 275 280 285
 Phe Ala Asn Leu Phe Thr Met Tyr Pro Arg Met Val Val Ser Ser His
 290 295 300
 Arg Ile Arg Glu Val Met Asp Met Pro Ile Ser Ile Asn Pro Asn Ala
 305 310 315 320
 Glu Gly Val Thr Asp Thr Lys Leu Lys Gly His Leu Glu Phe Asp Asn
 325 330 335
 Val Thr Phe Ala Tyr Pro Gly Glu Thr Glu Ser Pro Val Leu His Asp
 340 345 350
 Ile Ser Phe Lys Ala Lys Pro Gly Glu Thr Ile Ala Phe Ile Gly Ser
 355 360 365
 Thr Gly Ser Gly Lys Ser Ser Leu Val Asn Leu Ile Pro Arg Phe Tyr
 370 375 380
 Asp Val Thr Leu Gly Lys Ile Leu Val Asp Gly Val Asp Val Arg Asp
 385 390 395 400
 Tyr Asn Leu Lys Ser Leu Arg Gln Lys Ile Gly Phe Ile Pro Gln Lys
 405 410 415
 Ala Leu Leu Phe Thr Gly Thr Ile Gly Glu Asn Leu Lys Tyr Gly Lys
 420 425 430

Ala Asp Ala Thr Ile Asp Asp Leu Arg Gln Ala Val Asp Ile Ser Gln
 435 440 445
 Ala Lys Glu Phe Ile Glu Ser His Gln Glu Ala Phe Glu Thr His Leu
 450 455 460
 Ala Glu Gly Gly Ser Asn Leu Ser Gly Gly Gln Lys Gln Arg Leu Ser
 465 470 475 480
 Ile Ala Arg Ala Val Val Lys Asp Pro Asp Leu Tyr Ile Phe Asp Asp
 485 490 495
 Ser Phe Ser Ala Leu Asp Tyr Lys Thr Asp Ala Thr Leu Arg Ala Arg
 500 505 510
 Leu Lys Glu Val Thr Gly Asp Ser Thr Val Leu Ile Val Ala Gln Arg
 515 520 525
 Val Gly Thr Ile Met Asp Ala Asp Gln Ile Ile Val Leu Asp Glu Gly
 530 535 540
 Glu Ile Val Gly Arg Gly Thr His Ala Gln Leu Ile Glu Asn Asn Ala
 545 550 555 560
 Ile Tyr Arg Glu Ile Ala Glu Ser Gln Leu Lys Asn Gln Asn Leu Ser
 565 570 575
 Glu Gly Glu

<210> 12
 <211> 92
 <212> PRT
 <213> Streptococcus

<400> 12
 Met Arg Lys Lys Ser Val Phe Leu Arg Leu Trp Ser Tyr Leu Thr Arg
 1 5 10 15
 Tyr Lys Ala Thr Leu Phe Leu Ala Ile Phe Leu Lys Val Leu Ser Ser
 20 25 30
 Phe Met Ser Val Leu Glu Pro Phe Ile Leu Gly Leu Ala Ile Thr Glu
 35 40 45
 Leu Thr Ala Asn Leu Val Asp Met Ala Lys Gly Val Ser Gly Ala Glu
 50 55 60
 Leu Asn Val Pro Tyr Ile Ala Gly Ile Leu Ile Ile Tyr Phe Phe Arg
 65 70 75 80
 Gly Val Phe Tyr Glu Leu Gly Ser Tyr Gly Ser Asn
 85 90

<210> 13
 <211> 5215
 <212> DNA
 <213> Streptococcus

<220>
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 <221> CDS
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<222> (3252)...(2995)
<223> of complementary strand

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<223> of complementary strand

<221> CDS
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<223> of complementary strand

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  Phe Gly Ser Ala Leu Ser Thr Val Glu Val Lys Glu Ile Ile Ser
  1           5           10           15

gaa gaa aac ata tgg tta tat cgg ctc agt tgc tgc cat ttt act agc      95
  Glu Glu Asn Ile Trp Leu Tyr Arg Leu Ser Cys Cys His Phe Thr Ser
  20          25          30

tac tca tat tgg aag tta cca act tgg taagcatcat atg ggt cta gca      144
  Tyr Ser Tyr Trp Lys Leu Pro Thr Trp           Met Gly Leu Ala
  35          40

aca aag gac aat cag att gcc tat att gat gac agc aaa ggt aag gca      192
  Thr Lys Asp Asn Gln Ile Ala Tyr Ile Asp Asp Ser Lys Gly Lys Ala
  45          50          55          60

aaa gcc cct aaa aca aac aaa acg atg gat caa atc agt gct gaa gaa      240
  Lys Ala Pro Lys Thr Asn Lys Thr Met Asp Gln Ile Ser Ala Glu Glu
  65          70          75

ggc atc tct gct gaa cag atc gta gtc aaa att act gac caa ggc tat      288
  Gly Ile Ser Ala Glu Gln Ile Val Val Lys Ile Thr Asp Gln Gly Tyr
  80          85          90

gtg acc tca cac ggt gac cat tat cat ttt tac aat ggg aaa gtt cct      336
  Val Thr Ser His Gly Asp His Tyr His Phe Tyr Asn Gly Lys Val Pro
  95          100         105

tat gat gcg att att agt gaa gag ttg ttg atg acg gat cct aat tac      384
  Tyr Asp Ala Ile Ile Ser Glu Glu Leu Leu Met Thr Asp Pro Asn Tyr
  110         115         120

cgt ttt aaa caa tca gac gtt atc aat gaa atc tta gac ggt tac gtt      432
  Arg Phe Lys Gln Ser Asp Val Ile Asn Glu Ile Leu Asp Gly Tyr Val
  125         130         135         140

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att aaa gtc aat ggc aac tat tat gtt tac ctc aag cca ggt agt aag	480
Ile Lys Val Asn Gly Asn Tyr Tyr Val Tyr Leu Lys Pro Gly Ser Lys	
145 150 155	
cgc aaa aac att cga acc aaa caa caa att gct gag caa gta gcc aaa	528
Arg Lys Asn Ile Arg Thr Lys Gln Ile Ala Glu Gln Val Ala Lys	
160 165 170	
gga act aaa gaa gct aaa gaa aaa ggt tta gct caa gtg gcc cat ctc	576
Gly Thr Lys Glu Ala Lys Glu Lys Gly Leu Ala Gln Val Ala His Leu	
175 180 185	
agt aaa gaa gaa gtt gcg gca gtc aat gaa gca aaa aga caa gga cgc	624
Ser Lys Glu Glu Val Ala Ala Val Asn Glu Ala Lys Arg Gln Gly Arg	
190 195 200	
tat act aca gac gat ggc tat att ttt agt ccg aca gat atc att gat	672
Tyr Thr Asp Asp Gly Tyr Ile Phe Ser Pro Thr Asp Ile Ile Asp	
205 210 215 220	
gat tta gga gat gct tat tta gta cct cat ggt aat cac tat cat tat	720
Asp Leu Gly Asp Ala Tyr Leu Val Pro His Gly Asn His Tyr His Tyr	
225 230 235	
att cct aaa aag gat ttg tct cca agt gag cta gct gct gca caa gcc	768
Ile Pro Lys Lys Asp Leu Ser Pro Ser Glu Leu Ala Ala Gln Ala	
240 245 250	
tac tgg agt caa aaa caa ggt cga ggt gct aga ccg tct gat tac cgc	816
Tyr Trp Ser Gln Lys Gln Gly Arg Gly Ala Arg Pro Ser Asp Tyr Arg	
255 260 265	
ccg aca cca gcc cca ggt cgt agg aaa gcc cca att cct gat gtg acg	864
Pro Thr Pro Ala Pro Gly Arg Arg Lys Ala Pro Ile Pro Asp Val Thr	
270 275 280	
cct aac cct gga caa ggt cat cag cca gat aac ggt ggc tat cat cca	912
Pro Asn Pro Gly Gln Gly His Gln Pro Asp Asn Gly Gly Tyr His Pro	
285 290 295 300	
gcg cct cct agg cca aat gat gcg tca caa aac aaa cac caa aga gat	960
Ala Pro Pro Arg Pro Asn Asp Ala Ser Gln Asn Lys His Gln Arg Asp	
305 310 315	
gag ttt aaa gga aaa acc ttt aag gaa ctt tta gat caa cta cac cgt	1008
Glu Phe Lys Gly Lys Thr Phe Lys Glu Leu Leu Asp Gln Leu His Arg	
320 325 330	
ctt gat ttg aaa tac cgt cat gtg gaa gaa gat ggg ttg att ttt gaa	1056
Leu Asp Leu Lys Tyr Arg His Val Glu Glu Asp Gly Leu Ile Phe Glu	
335 340 345	
ccg act caa gtg atc aaa tca aac gct ttt ggg tat gtg gtg cct cat	1104
Pro Thr Gln Val Ile Lys Ser Asn Ala Phe Gly Tyr Val Val Pro His	
350 355 360	

gga gat cat tat cat att atc cca aga agt cag tta tca cct ctt gaa	1152
Gly Asp His Tyr His Ile Ile Pro Arg Ser Gln Leu Ser Pro Leu Glu	
365 370 375 380	
atg gaa tta gca gat cga tac tta gct ggc caa act gag gac aat gac	1200
Met Glu Leu Ala Asp Arg Tyr Leu Ala Gly Gln Thr Glu Asp Asn Asp	
385 390 395	
tca ggt tca gag cac tca aaa cca tca gat aaa gaa gtg aca cat acc	1248
Ser Gly Ser Glu His Ser Lys Pro Ser Asp Lys Glu Val Thr His Thr	
400 405 410	
ttt ctt ggt cat cgc atc aaa gct tac gga aaa ggc tta gat ggt aaa	1296
Phe Leu Gly His Arg Ile Lys Ala Tyr Gly Lys Gly Leu Asp Gly Lys	
415 420 425	
cca tat gat acg agt gat gct tat gtt ttt agt aaa gaa tcc att cat	1344
Pro Tyr Asp Thr Ser Asp Ala Tyr Val Phe Ser Lys Glu Ser Ile His	
430 435 440	
tca gtg gat aaa tca gga gtt aca gct aaa cac gga gat cat ttc cac	1392
Ser Val Asp Lys Ser Gly Val Thr Ala Lys His Gly Asp His Phe His	
445 450 455 460	
tat ata gga ttt gga gaa ctt gaa caa tat gag ttg gat gag gtc gct	1440
Tyr Ile Gly Phe Gly Glu Leu Glu Gln Tyr Glu Leu Asp Glu Val Ala	
465 470 475	
aac tgg gtg aaa gca aaa ggt caa gct gat gag ctt gct gct gct ttg	1488
Asn Trp Val Lys Ala Lys Gly Gln Ala Asp Glu Leu Ala Ala Leu	
480 485 490	
gat cag gaa caa ggc aaa gaa aaa cca ctc ttt gac act aaa aaa gtg	1536
Asp Gln Glu Gln Gly Lys Glu Lys Pro Leu Phe Asp Thr Lys Lys Val	
495 500 505	
agt cgc aaa gta aca aaa gat ggt aaa gtg ggc tat atg atg cca aaa	1584
Ser Arg Lys Val Thr Lys Asp Gly Lys Val Gly Tyr Met Met Pro Lys	
510 515 520	
gat ggt aag gac tat ttc tat gct cgt gat caa ctt gat ttg act cag	1632
Asp Gly Lys Asp Tyr Phe Tyr Ala Arg Asp Gln Leu Asp Leu Thr Gln	
525 530 535 540	
att gcc ttt gcc gaa caa gaa cta atg ctt aaa gat aag aag cat tac	1680
Ile Ala Phe Ala Glu Gln Glu Leu Met Leu Lys Asp Lys Lys His Tyr	
545 550 555	
cgt tat gac att gtt gac aca ggt att gag cca cga ctt gct gta gat	1728
Arg Tyr Asp Ile Val Asp Thr Gly Ile Glu Pro Arg Leu Ala Val Asp	
560 565 570	
gtg tca agt ctg ccg atg cat gct ggt aat gct act tac gat act gga	1776
Val Ser Ser Leu Pro Met His Ala Gly Asn Ala Thr Tyr Asp Thr Gly	
575 580 585	

agt tcg ttt gtt atc cca cat att gat cat atc cat gtc gtt ccg tat		1824
Ser Phe Val Ile Pro His Ile Asp His Ile His Val Val Pro Tyr		
590	595	600
tca tgg ttg acg cgc gat cag att gca aca gtc aag tat gtg atg caa		1872
Ser Trp Leu Thr Arg Asp Gln Ile Ala Thr Val Lys Tyr Val Met Gln		
605	610	615
620		
cac ccc gaa gtt cgt ccg gat gta tgg tct aag cca ggg cat gaa gag		1920
His Pro Glu Val Arg Pro Asp Val Trp Ser Lys Pro Gly His Glu Glu		
625	630	635
tca ggt tcg gtc att cca aat gtt acg cct ctt gat aaa cgt gct ggt		1968
Ser Gly Ser Val Ile Pro Asn Val Thr Pro Leu Asp Lys Arg Ala Gly		
640	645	650
atg cca aac tgg caa att atc cat tct gct gaa gaa gtt caa aaa gcc		2016
Met Pro Asn Trp Gln Ile Ile His Ser Ala Glu Glu Val Gln Lys Ala		
655	660	665
cta gca gaa ggt cgt ttt gca aca cca gac ggc tat att ttc gat cca		2064
Leu Ala Glu Gly Arg Phe Ala Thr Pro Asp Gly Tyr Ile Phe Asp Pro		
670	675	680
cga gat gtt ttg gcc aaa gaa act ttt gta tgg aaa gat ggc tcc ttt		2112
Arg Asp Val Leu Ala Lys Glu Thr Phe Val Trp Lys Asp Gly Ser Phe		
685	690	695
700		
agc atc cca aga gca gat ggc agt tca ttg aga acc att aat aaa tct		2160
Ser Ile Pro Arg Ala Asp Gly Ser Ser Leu Arg Thr Ile Asn Lys Ser		
705	710	715
gat cta tcc caa gct gag tgg caa caa gct caa gag tta ttg gca aag		2208
Asp Leu Ser Gln Ala Glu Trp Gln Gln Ala Gln Glu Leu Leu Ala Lys		
720	725	730
aaa aat act ggt gat gct act gat acg gat aaa ccc aaa gaa aag caa		2256
Lys Asn Thr Gly Asp Ala Thr Asp Thr Asp Lys Pro Lys Glu Lys Gln		
735	740	745
cag gca gat aag agc aat gaa aac caa cag cca agt gaa gcc agt aaa		2304
Gln Ala Asp Lys Ser Asn Glu Asn Gln Gln Pro Ser Glu Ala Ser Lys		
750	755	760
gaa gaa aaa gaa tca gat gac ttt ata gac agt tta cca gac tat ggt		2352
Glu Glu Lys Glu Ser Asp Asp Phe Ile Asp Ser Leu Pro Asp Tyr Gly		
765	770	775
780		
cta gat aga gca acc cta gaa gat cat atc aat caa tta gca caa aaa		2400
Leu Asp Arg Ala Thr Leu Glu Asp His Ile Asn Gln Leu Ala Gln Lys		
785	790	795
gct aat atc gat cct aag tat ctc att ttc caa cca gaa ggt gtc caa		2448
Ala Asn Ile Asp Pro Lys Tyr Leu Ile Phe Gln Pro Glu Gly Val Gln		
800	805	810

ttt tat aat aaa aat ggt gaa ttg gta act tat gat atc aag aca ctt	2496
Phe Tyr Asn Lys Asn Gly Glu Leu Val Thr Tyr Asp Ile Lys Thr Leu	
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caa caa ata aac cct taacccaaag aagatctcat tgtaaagca ctgcggcgc	2551
Gln Gln Ile Asn Pro	
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<211> 40	
<212> PRT	

<213> Streptococcus

<400> 14

Phe	Gly	Ser	Ala	Leu	Ser	Thr	Val	Glu	Val	Lys	Glu	Ile	Ile	Ser	Glu
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Glu	Asn	Ile	Trp	Leu	Tyr	Arg	Leu	Ser	Cys	Cys	His	Phe	Thr	Ser	Tyr
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Ser	Tyr	Trp	Lys	Leu	Pro	Thr	Trp								
								35				40			

<210> 15

<211> 793

<212> PRT

<213> Streptococcus

<400> 15

Met	Gly	Leu	Ala	Thr	Lys	Asp	Asn	Gln	Ile	Ala	Tyr	Ile	Asp	Asp	Ser
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Lys	Gly	Lys	Ala	Lys	Ala	Pro	Lys	Thr	Asn	Lys	Thr	Met	Asp	Gln	Ile
								20		25		30			
Ser	Ala	Glu	Glu	Gly	Ile	Ser	Ala	Glu	Gln	Ile	Val	Val	Lys	Ile	Thr
								35		40		45			
Asp	Gln	Gly	Tyr	Val	Thr	Ser	His	Gly	Asp	His	Tyr	His	Phe	Tyr	Asn
								50		55		60			
Gly	Lys	Val	Pro	Tyr	Asp	Ala	Ile	Ile	Ser	Glu	Glu	Leu	Leu	Met	Thr
								65		70		75		80	
Asp	Pro	Asn	Tyr	Arg	Phe	Lys	Gln	Ser	Asp	Val	Ile	Asn	Glu	Ile	Leu
								85		90		95			
Asp	Gly	Tyr	Val	Ile	Lys	Val	Asn	Gly	Asn	Tyr	Tyr	Val	Tyr	Leu	Lys
								100		105		110			
Pro	Gly	Ser	Lys	Arg	Lys	Asn	Ile	Arg	Thr	Lys	Gln	Gln	Ile	Ala	Glu
								115		120		125			
Gln	Val	Ala	Lys	Gly	Thr	Lys	Glu	Ala	Lys	Glu	Lys	Gly	Leu	Ala	Gln
								130		135		140			
Val	Ala	His	Leu	Ser	Lys	Glu	Glu	Val	Ala	Ala	Val	Asn	Glu	Ala	Lys
								145		150		155		160	
Arg	Gln	Gly	Arg	Tyr	Thr	Thr	Asp	Asp	Gly	Tyr	Ile	Phe	Ser	Pro	Thr
								165		170		175			
Asp	Ile	Ile	Asp	Asp	Leu	Gly	Asp	Ala	Tyr	Leu	Val	Pro	His	Gly	Asn
								180		185		190			
His	Tyr	His	Tyr	Ile	Pro	Lys	Lys	Asp	Leu	Ser	Pro	Ser	Glu	Leu	Ala
								195		200		205			
Ala	Ala	Gln	Ala	Tyr	Trp	Ser	Gln	Lys	Gln	Gly	Arg	Gly	Ala	Arg	Pro
								210		215		220			
Ser	Asp	Tyr	Arg	Pro	Thr	Pro	Ala	Pro	Gly	Arg	Arg	Lys	Ala	Pro	Ile
								225		230		235		240	
Pro	Asp	Val	Thr	Pro	Asn	Pro	Gly	Gln	Gly	His	Gln	Pro	Asp	Asn	Gly
								245		250		255			
Gly	Tyr	His	Pro	Ala	Pro	Pro	Arg	Pro	Asn	Asp	Ala	Ser	Gln	Asn	Lys
								260		265		270			
His	Gln	Arg	Asp	Glu	Phe	Lys	Gly	Lys	Thr	Phe	Lys	Glu	Leu	Leu	Asp
								275		280		285			
Gln	Leu	His	Arg	Leu	Asp	Leu	Lys	Tyr	Arg	His	Val	Glu	Glu	Asp	Gly
								290		295		300			
Leu	Ile	Phe	Glu	Pro	Thr	Gln	Val	Ile	Lys	Ser	Asn	Ala	Phe	Gly	Tyr
								305		310		315		320	

Val Val Pro His Gly Asp His Tyr His Ile Ile Pro Arg Ser Gln Leu
 325 330 335
 Ser Pro Leu Glu Met Glu Leu Ala Asp Arg Tyr Leu Ala Gly Gln Thr
 340 345 350
 Glu Asp Asn Asp Ser Gly Ser Glu His Ser Lys Pro Ser Asp Lys Glu
 355 360 365
 Val Thr His Thr Phe Leu Gly His Arg Ile Lys Ala Tyr Gly Lys Gly
 370 375 380
 Leu Asp Gly Lys Pro Tyr Asp Thr Ser Asp Ala Tyr Val Phe Ser Lys
 385 390 395 400
 Glu Ser Ile His Ser Val Asp Lys Ser Gly Val Thr Ala Lys His Gly
 405 410 415
 Asp His Phe His Tyr Ile Gly Phe Gly Glu Leu Glu Gln Tyr Glu Leu
 420 425 430
 Asp Glu Val Ala Asn Trp Val Lys Ala Lys Gly Gln Ala Asp Glu Leu
 435 440 445
 Ala Ala Ala Leu Asp Gln Glu Gln Gly Lys Glu Lys Pro Leu Phe Asp
 450 455 460
 Thr Lys Lys Val Ser Arg Lys Val Thr Lys Asp Gly Lys Val Gly Tyr
 465 470 475 480
 Met Met Pro Lys Asp Gly Lys Asp Tyr Phe Tyr Ala Arg Asp Gln Leu
 485 490 495
 Asp Leu Thr Gln Ile Ala Phe Ala Glu Gln Glu Leu Met Leu Lys Asp
 500 505 510
 Lys Lys His Tyr Arg Tyr Asp Ile Val Asp Thr Gly Ile Glu Pro Arg
 515 520 525
 Leu Ala Val Asp Val Ser Ser Leu Pro Met His Ala Gly Asn Ala Thr
 530 535 540
 Tyr Asp Thr Gly Ser Ser Phe Val Ile Pro His Ile Asp His Ile His
 545 550 555 560
 Val Val Pro Tyr Ser Trp Leu Thr Arg Asp Gln Ile Ala Thr Val Lys
 565 570 575
 Tyr Val Met Gln His Pro Glu Val Arg Pro Asp Val Trp Ser Lys Pro
 580 585 590
 Gly His Glu Glu Ser Gly Ser Val Ile Pro Asn Val Thr Pro Leu Asp
 595 600 605
 Lys Arg Ala Gly Met Pro Asn Trp Gln Ile Ile His Ser Ala Glu Glu
 610 615 620
 Val Gln Lys Ala Leu Ala Glu Gly Arg Phe Ala Thr Pro Asp Gly Tyr
 625 630 635 640
 Ile Phe Asp Pro Arg Asp Val Leu Ala Lys Glu Thr Phe Val Trp Lys
 645 650 655
 Asp Gly Ser Phe Ser Ile Pro Arg Ala Asp Gly Ser Ser Leu Arg Thr
 660 665 670
 Ile Asn Lys Ser Asp Leu Ser Gln Ala Glu Trp Gln Gln Ala Gln Glu
 675 680 685
 Leu Leu Ala Lys Lys Asn Thr Gly Asp Ala Thr Asp Thr Asp Lys Pro
 690 695 700
 Lys Glu Lys Gln Gln Ala Asp Lys Ser Asn Glu Asn Gln Gln Pro Ser
 705 710 715 720
 Glu Ala Ser Lys Glu Glu Lys Glu Ser Asp Asp Phe Ile Asp Ser Leu
 725 730 735
 Pro Asp Tyr Gly Leu Asp Arg Ala Thr Leu Glu Asp His Ile Asn Gln
 740 745 750
 Leu Ala Gln Lys Ala Asn Ile Asp Pro Lys Tyr Leu Ile Phe Gln Pro
 755 760 765

Glu Gly Val Gln Phe Tyr Asn Lys Asn Gly Glu Leu Val Thr Tyr Asp
 770 775 780
 Ile Lys Thr Leu Gln Gln Ile Asn Pro
 785 790

<210> 16
 <211> 715
 <212> PRT
 <213> Streptococcus

<400> 16

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 Ile Leu Asp Gly Tyr Val Ile Lys Val Asn Gly Asn Tyr Tyr Val Tyr
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 Leu Lys Pro Gly Ser Lys Arg Lys Asn Ile Arg Thr Lys Gln Gln Ile
 35 40 45
 Ala Glu Gln Val Ala Lys Gly Thr Lys Glu Ala Lys Glu Lys Gly Leu
 50 55 60
 Ala Gln Val Ala His Leu Ser Lys Glu Glu Val Ala Ala Val Asn Glu
 65 70 75 80
 Ala Lys Arg Gln Gly Arg Tyr Thr Thr Asp Asp Gly Tyr Ile Phe Ser
 85 90 95
 Pro Thr Asp Ile Ile Asp Asp Leu Gly Asp Ala Tyr Leu Val Pro His
 100 105 110
 Gly Asn His Tyr His Tyr Ile Pro Lys Lys Asp Leu Ser Pro Ser Glu
 115 120 125
 Leu Ala Ala Ala Gln Ala Tyr Trp Ser Gln Lys Gln Gly Arg Gly Ala
 130 135 140
 Arg Pro Ser Asp Tyr Arg Pro Thr Pro Ala Pro Gly Arg Arg Lys Ala
 145 150 155 160
 Pro Ile Pro Asp Val Thr Pro Asn Pro Gly Gln Gly His Gln Pro Asp
 165 170 175
 Asn Gly Gly Tyr His Pro Ala Pro Pro Arg Pro Asn Asp Ala Ser Gln
 180 185 190
 Asn Lys His Gln Arg Asp Glu Phe Lys Gly Lys Thr Phe Lys Glu Leu
 195 200 205
 Leu Asp Gln Leu His Arg Leu Asp Leu Lys Tyr Arg His Val Glu Glu
 210 215 220
 Asp Gly Leu Ile Phe Glu Pro Thr Gln Val Ile Lys Ser Asn Ala Phe
 225 230 235 240
 Gly Tyr Val Val Pro His Gly Asp His Tyr His Ile Ile Pro Arg Ser
 245 250 255
 Gln Leu Ser Pro Leu Glu Met Glu Leu Ala Asp Arg Tyr Leu Ala Gly
 260 265 270
 Gln Thr Glu Asp Asn Asp Ser Gly Ser Glu His Ser Lys Pro Ser Asp
 275 280 285
 Lys Glu Val Thr His Thr Phe Leu Gly His Arg Ile Lys Ala Tyr Gly
 290 295 300
 Lys Gly Leu Asp Gly Lys Pro Tyr Asp Thr Ser Asp Ala Tyr Val Phe
 305 310 315 320
 Ser Lys Glu Ser Ile His Ser Val Asp Lys Ser Gly Val Thr Ala Lys
 325 330 335
 His Gly Asp His Phe His Tyr Ile Gly Phe Gly Glu Leu Glu Gln Tyr
 340 345 350

Glu Leu Asp Glu Val Ala Asn Trp Val Lys Ala Lys Gly Gln Ala Asp
 355 360 365
 Glu Leu Ala Ala Ala Leu Asp Gln Glu Gln Gly Lys Glu Lys Pro Leu
 370 375 380
 Phe Asp Thr Lys Lys Val Ser Arg Lys Val Thr Lys Asp Gly Lys Val
 385 390 395 400
 Gly Tyr Met Met Pro Lys Asp Gly Lys Asp Tyr Phe Tyr Ala Arg Asp
 405 410 415
 Gln Leu Asp Leu Thr Gln Ile Ala Phe Ala Glu Gln Glu Leu Met Leu
 420 425 430
 Lys Asp Lys His Tyr Arg Tyr Asp Ile Val Asp Thr Gly Ile Glu
 435 440 445
 Pro Arg Leu Ala Val Asp Val Ser Ser Leu Pro Met His Ala Gly Asn
 450 455 460
 Ala Thr Tyr Asp Thr Gly Ser Ser Phe Val Ile Pro His Ile Asp His
 465 470 475 480
 Ile His Val Val Pro Tyr Ser Trp Leu Thr Arg Asp Gln Ile Ala Thr
 485 490 495
 Val Lys Tyr Val Met Gln His Pro Glu Val Arg Pro Asp Val Trp Ser
 500 505 510
 Lys Pro Gly His Glu Glu Ser Gly Ser Val Ile Pro Asn Val Thr Pro
 515 520 525
 Leu Asp Lys Arg Ala Gly Met Pro Asn Trp Gln Ile Ile His Ser Ala
 530 535 540
 Glu Glu Val Gln Lys Ala Leu Ala Glu Gly Arg Phe Ala Thr Pro Asp
 545 550 555 560
 Gly Tyr Ile Phe Asp Pro Arg Asp Val Leu Ala Lys Glu Thr Phe Val
 565 570 575
 Trp Lys Asp Gly Ser Phe Ser Ile Pro Arg Ala Asp Gly Ser Ser Leu
 580 585 590
 Arg Thr Ile Asn Lys Ser Asp Leu Ser Gln Ala Glu Trp Gln Gln Ala
 595 600 605
 Gln Glu Leu Leu Ala Lys Lys Asn Thr Gly Asp Ala Thr Asp Thr Asp
 610 615 620
 Lys Pro Lys Glu Lys Gln Gln Ala Asp Lys Ser Asn Glu Asn Gln Gln
 625 630 635 640
 Pro Ser Glu Ala Ser Lys Glu Glu Lys Glu Ser Asp Asp Phe Ile Asp
 645 650 655
 Ser Leu Pro Asp Tyr Gly Leu Asp Arg Ala Thr Leu Glu Asp His Ile
 660 665 670
 Asn Gln Leu Ala Gln Lys Ala Asn Ile Asp Pro Lys Tyr Leu Ile Phe
 675 680 685
 Gln Pro Glu Gly Val Gln Phe Tyr Asn Lys Asn Gly Glu Leu Val Thr
 690 695 700
 Tyr Asp Ile Lys Thr Leu Gln Gln Ile Asn Pro
 705 710 715

<210> 17
 <211> 77
 <212> PRT
 <213> Streptococcus

<400> 17

Met His Ser Phe Ser Asn Pro Gly Tyr Pro Tyr Asp Asn Ala Val Thr
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Glu Ala Phe Phe Lys Tyr Leu Lys His Arg Gln Ile Asn Arg Lys His
 20 25 30
 Tyr Gln Asn Ile Lys Gln Val Gln Leu Asp Cys Phe Glu Tyr Ile Glu
 35 40 45
 Asn Phe Tyr Asn Asn Tyr Asn Pro His Thr Ala Asn Leu Gly Leu Thr
 50 55 60
 Pro Asn Gln Lys Glu Glu Asn Tyr Phe Asn Ala Ile Lys
 65 70 75

<210> 18
 <211> 86
 <212> PRT
 <213> Streptococcus

<400> 18
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 Ser Arg Lys Gly Thr Pro Ala Asp Asn Ala Cys Ile Glu Trp Phe His
 20 25 30
 Thr Val Leu Lys Thr Glu Thr Phe Tyr Phe His Asn Arg Arg Lys Tyr
 35 40 45
 Asn Lys Asp Ser Ile Thr Asn Ile Val Lys Asn Tyr Ile Thr Phe Tyr
 50 55 60
 Asn Glu Thr Arg Ile Gln Gln Arg Leu Asn Asp Gln Ser Pro Val Gln
 65 70 75 80
 Tyr Arg Lys Leu Ile Ala
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<210> 19
 <211> 126
 <212> PRT
 <213> Streptococcus

<400> 19
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 Lys Lys Ile His Gly Leu Thr Val Asn Thr Lys Lys Val Tyr Arg Ile
 20 25 30
 Met Lys Asn Asn Gly Trp Leu Cys Arg Thr Arg Thr Lys Lys Val Pro
 35 40 45
 Asn Leu Gly Lys Ala Tyr Tyr Leu Thr Asp Asn Lys Leu Ser Arg Asp
 50 55 60
 Phe His Ala Asp Lys Pro Lys Glu Lys Leu Val Thr Asp Ile Thr Tyr
 65 70 75 80
 Leu Tyr Phe Gly Asn Cys Lys Leu Tyr Leu Ser Ser Ile Met Asn Leu
 85 90 95
 Tyr Asn Arg Glu Ile Ile Ala Tyr Thr Ile Ser Asp Cys Gln Asp Thr
 100 105 110
 Asp Phe Val Leu Asp Thr Leu Asn Gln Leu Lys Leu Pro Lys
 115 120 125

<210> 20
 <211> 96
 <212> PRT
 <213> Streptococcus

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 Met Lys Lys Ala Gly Lys Ser Asn Arg Val Ile Met Glu Thr Leu Gly
 20 25 30
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 35 40 45
 Glu Glu Leu Tyr Arg Phe His Gln Gly Val Gly Lys Gln Tyr Thr Tyr
 50 55 60
 Gly Lys Gly Leu Glu His Leu Ser Glu Val Glu Gln Leu Gln Leu Gln
 65 70 75 80
 Val Asp Leu Leu Lys Tyr Arg Gly Leu Ile Arg Lys Ser Ile Lys
 85 90 95

<210> 21
 <211> 288
 <212> PRT
 <213> streptococcus

<400> 21
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 35 40 45
 Val Ser Glu Thr Glu Phe Glu Glu Thr Ile Lys Arg Ile Phe Leu Asp
 50 55 60
 Ser Glu Ser Arg Tyr Gly Ser Arg Lys Ile Lys Ile Cys Leu Asn Asn
 65 70 75 80
 Glu Gly Ile Thr Leu Ser Arg Arg Arg Ile Arg Arg Ile Met Lys Arg
 85 90 95
 Leu Asn Leu Val Ser Val Tyr Gln Lys Ala Thr Phe Lys Pro His Ser
 100 105 110
 Arg Gly Lys Asn Glu Ala Pro Ile Pro Asn His Leu Asp Arg Gln Phe
 115 120 125
 Lys Gln Glu Arg Pro Leu Gln Ala Leu Val Thr Asp Leu Thr Tyr Val
 130 135 140
 Arg Val Gly Asn Arg Trp Ala Tyr Val Cys Leu Ile Ile Asp Leu Tyr
 145 150 155 160
 Asn Arg Glu Ile Ile Gly Leu Ser Leu Gly Trp His Lys Thr Ala Glu
 165 170 175
 Leu Val Lys Gln Ala Ile Gln Ser Ile Pro Tyr Ala Leu Thr Lys Val
 180 185 190
 Lys Met Phe His Ser Asp Arg Gly Lys Glu Phe Asp Asn Gln Leu Ile
 195 200 205
 Asp Glu Ile Leu Glu Ala Phe Gly Ile Thr Arg Ser Leu Ser Gln Ala
 210 215 220
 Gly Tyr Pro Tyr Asp Asn Ala Val Ala Glu Ser Thr Tyr Arg Ala Phe
 225 230 235 240
 Lys Ile Glu Phe Val Tyr Gln Glu Thr Phe Gln Leu Leu Glu Glu Leu
 245 250 255
 Ala Leu Lys Thr Lys Asp Tyr Val His Trp Trp Asn Tyr His Arg Ile
 260 265 270
 His Gly Ser Leu Asn Tyr Gln Thr Pro Met Thr Lys Arg Leu Ile Ala
 275 280 285

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<210> 22
<211> 5058
<212> DNA
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<220>
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<221> CDS
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<400> 22
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 1           5           10           15

gtt tat ggt aaa tct gct cat ggt tca aca cca caa gaa ggt gtt aat      96
Val Tyr Gly Lys Ser Ala His Gly Ser Thr Pro Gln Glu Gly Val Asn
 20          25          30

ggg gcg act tat tta gct ctt tat cta agt caa ttt gat ttt gaa ggt      144
Gly Ala Thr Tyr Leu Ala Leu Tyr Leu Ser Gln Phe Asp Phe Glu Gly
 35          40          45

cct gct cgt gct ttc tta gat gtt aca gcc aac att att cac gaa gac      192
Pro Ala Arg Ala Phe Leu Asp Val Thr Ala Asn Ile Ile His Glu Asp
 50          55          60

ttc tca ggt gaa aaa ctt gga gta gct tat gaa gat gac tgt atg gga      240
Phe Ser Gly Glu Lys Leu Gly Val Ala Tyr Glu Asp Asp Cys Met Gly
 65          70          75          80

cca ttg agc atg aat gca ggt gtc ttc cag ttt gat gaa act aat gat      288
Pro Leu Ser Met Asn Ala Gly Val Phe Gln Phe Asp Glu Thr Asn Asp
 85          90          95

gat aat act atc gct ctt aat ttc cgt tac cca caa ggg aca gat gct      336
Asp Asn Thr Ile Ala Leu Asn Phe Arg Tyr Pro Gln Gly Thr Asp Ala
 100         105         110

aaa act atc caa act aag ctt gag aaa ctt aac gga gtt gaa aaa gtg      384
Lys Thr Ile Gln Thr Lys Leu Glu Lys Leu Asn Gly Val Glu Lys Val
 115         120         125

act ctt tct gac cat gaa cac aca cca cac tat gta cct atg gac gat      432
Thr Leu Ser Asp His Glu His Thr Pro His Tyr Val Pro Met Asp Asp
 130         135         140

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gaa tta gta tca acc tta cta gct gtc tat gaa aag caa act ggt ctt	480
Glu Leu Val Ser Thr Leu Leu Ala Val Tyr Glu Lys Gln Thr Gly Leu	
145 150 155 160	
aaa gga cat gaa cag gtt att ggt ggt ggg aca ttt ggt cgc tta ctt	528
Lys Gly His Glu Gln Val Ile Gly Gly Thr Phe Gly Arg Leu Leu	
165 170 175	
gaa cgg ggt gtt gca tac ggt gcc atg ttc cca gga gat gaa aac act	576
Glu Arg Gly Val Ala Tyr Gly Ala Met Phe Pro Gly Asp Glu Asn Thr	
180 185 190	
atg cat caa gct aat gag tac atg cct tta gaa aat att ttc cgt tcg	624
Met His Gln Ala Asn Glu Tyr Met Pro Leu Glu Asn Ile Phe Arg Ser	
195 200 205	
gct gct atc tac gca gaa gct atc tat gaa tta atc aaa taaaataatc	673
Ala Ala Ile Tyr Ala Glu Ala Ile Tyr Glu Leu Ile Lys	
210 215 220	
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Lys Ala Ile Lys Ser Asp Ser Gln Asn Gln Asn Tyr Thr Glu Asn Gly	
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Ile Asp Pro Leu Phe Ala Ala Pro Lys Thr Ala Arg Ile Asn Ile Val	
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Gly Gln Ala Pro Gly Leu Lys Thr Gln Glu Ala Arg Leu Tyr Trp Lys	
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Asp Lys Ser Gly Asp Arg Leu Arg Gln Trp Leu Gly Val Asp Glu Glu	
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Thr Phe Tyr His Ser Gly Lys Phe Ala Val Leu Pro Leu Asp Phe Tyr	
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Tyr Pro Gly Lys Gly Lys Ser Gly Asp Leu Pro Pro Arg Lys Gly Phe	
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Ala Glu Lys Trp His Pro Leu Ile Leu Lys Glu Met Pro Asn Val Gln	
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Ser Ala His Lys Asn Leu Thr Glu Thr Val Lys Ala Tyr Lys Asp Tyr	
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Trp Leu Lys Lys Asn Pro Trp Phe Glu Lys Asp Leu Ile Val Asp Leu	
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caa aag ata gta gca gat att tta aaa gat taaggatagg agttggc atg	1364
Gln Lys Ile Val Ala Asp Ile Leu Lys Asp	
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Arg Asp Asn His Leu His Thr Tyr Phe Ser Tyr Asp Cys Gln Thr Ala	
420 425 430	
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Phe Glu Asp Tyr Ile Asn Gly Phe Thr Gly Glu Phe Ile Thr Thr Glu	
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His Phe Asp Leu Ser Asn Pro Tyr Thr Gly Gln Asp Asp Val Pro Asp	
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Tyr Ser Ala Tyr Cys Gln Lys Ile Asp Tyr Leu Asn Gln Lys Tyr Gly	
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Asn Arg Phe Lys Lys Gly Ile Glu Ile Gly Tyr Phe Lys Asp Arg Glu	
485 490 495	
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Ser Asp Ile Leu Asp Tyr Leu Lys Asn Lys Glu Phe Asp Leu Lys Leu	
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Leu Ser Ile His His Asn Gly Arg Tyr Asp Tyr Leu Gln Glu Glu Ala	
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Val Ala Ser Val Thr Thr Gly Val Cys Ile Phe Leu His Ser Pro Gln	
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Val Phe Ala Glu Glu Val Ser Val Ser Pro Ala Thr Thr Ala Ile Ala	
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Asp Asp Ile Asn Ser Asn Ser Glu Thr Val Val Thr Pro Ser Asp Met	
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Pro Asp Thr Lys Gln Leu Val Ser Asp Glu Thr Asp Thr Gln Lys Gly	
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Val Thr Glu Pro Asp Lys Ala Thr Ser Leu Leu Glu Glu Asn Lys Gly	
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Pro Val Ser Asp Lys Asn Thr Leu Asp Leu Lys Val Ala Pro Ser Thr	
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Leu Gln Asn Thr Pro Asp Lys Thr Ser Gln Ala Ile Gly Ala Pro Ser	
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Pro Thr Leu Lys Val Ala Asn Gln Ala Pro Arg Ile Glu Asn Gly Tyr	
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Phe Arg Leu His Leu Lys Glu Leu Pro Gln Gly His Pro Val Glu Ser	
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Thr Gly Leu Trp Ile Trp Gly Asp Val Asp Gln Pro Ser Ser Asn Trp	
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cca aat ggt gct atc cct atg act gat gct aag aaa gat gat tac ggt	2907
Pro Asn Gly Ala Ile Pro Met Thr Asp Ala Lys Lys Asp Asp Tyr Gly	
740 745 750 755	

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aat gct ata caa att tct gat atc act ctc gat act agt aaa tct ctt Asn Ala Ile Gln Ile Ser Asp Ile Thr Leu Asp Thr Ser Lys Ser Leu 965 970 975	3579

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Leu Ile Ile Lys Gly Asp Phe Asn Pro Lys Gln Gly His Phe Asn Ile	
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Ser Tyr Asn Gly Asn Asn Val Met Thr Arg Gln Ser Trp Glu Phe Lys	
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Asp Gln Leu Tyr Ala Tyr Ser Gly Asn Leu Gly Ala Val Leu Asn Gln	
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Asp Gly Ser Lys Val Glu Ala Ser Leu Trp Ser Pro Ser Ala Asp Ser	
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Val Thr Met Ile Ile Tyr Asp Lys Asp Asn Gln Asn Arg Val Val Ala	
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Thr Thr Pro Leu Val Lys Asn Asn Lys Gly Val Trp Gln Thr Ile Leu	
1060 1065 1070 1075	
gat act aaa tta ggt att aaa aac tat act ggt tac tat tat ctt tac	3915
Asp Thr Lys Leu Gly Ile Lys Asn Tyr Thr Gly Tyr Tyr Tyr Leu Tyr	
1080 1085 1090	
gaa ata aaa aga ggt aag gat aag gtt aag att tta gat cct tat gca	3963
Glu Ile Lys Arg Gly Lys Asp Lys Val Lys Ile Leu Asp Pro Tyr Ala	
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Lys Ser Leu Ala Glu Trp Asp Ser Asn Thr Val Asn Asp Asp Ile Lys	
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Leu Ser Phe Ala Lys Ile Ala Asn Phe Lys Gly Arg Gln Asp Ala Val	
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Ile Tyr Glu Ala His Val Arg Asp Phe Thr Ser Asp Arg Ser Leu Asp	
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Gly Lys Leu Lys Asn Gln Phe Gly Thr Phe Ala Ala Phe Ser Glu Lys	
1175 1180 1185	
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1190 1195 1200	

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Val Leu Ser Tyr Phe Tyr Val Asn Glu Met Asp Lys Ser Arg Ser Thr	
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Ala Tyr Thr Ser Ser Asp Asn Asn Tyr Asn Trp Gly Tyr Asp Pro Gln	
1220 1225 1230 1235	
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Ser Tyr Phe Ala Leu Ser Gly Met Tyr Ser Glu Lys Pro Lys Asp Pro	
1240 1245 1250	
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Ser Ala Arg Ile Ala Glu Leu Lys Gln Leu Ile His Asp Ile His Lys	
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Arg Gly Met Gly Val Ile Leu Asp Val Val Tyr Asn His Thr Ala Lys	
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Thr Tyr Leu Phe Glu Asp Ile Glu Pro Asn Tyr Tyr His Phe Met Asn	
1285 1290 1295	
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Thr Ser Glu Phe Lys Val Asp Gly Phe Arg Phe Asp Met Met Gly Asp	
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Asn Pro Asn Met Ile Met Ile Gly Glu Gly Trp Arg Thr Phe Gln Gly	
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Asp Gln Gly Gln Pro Val Lys Pro Ala Asp Gln Asp Trp Met Lys Ser	
1380 1385 1390 1395	
acc gat aca gtt ggc gtc ttt tca gat gat att cgt aat agc ttg aaa	4875
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Ser Gly Phe Pro Asn Glu Gly Thr Pro Ala Phe Ile Thr Gly Gly Pro	
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 Asp Asn Thr Ile Ala Leu Asn Phe Arg Tyr Pro Gln Gly Thr Asp Ala
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 Lys Thr Ile Gln Thr Lys Leu Glu Lys Leu Asn Gly Val Glu Lys Val
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 Thr Leu Ser Asp His Glu His Thr Pro His Tyr Val Pro Met Asp Asp
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 Glu Leu Val Ser Thr Leu Leu Ala Val Tyr Glu Lys Gln Thr Gly Leu
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 Lys Gly His Glu Gln Val Ile Gly Gly Thr Phe Gly Arg Leu Leu
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 Glu Arg Gly Val Ala Tyr Gly Ala Met Phe Pro Gly Asp Glu Asn Thr
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 Gln Trp Leu Gly Val Asp Glu Glu Thr Phe Tyr His Ser Gly Lys Phe
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 Ala Val Leu Pro Leu Asp Phe Tyr Tyr Pro Gly Lys Gly Lys Ser Gly
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 Asp Leu Pro Pro Arg Lys Gly Phe Ala Glu Lys Trp His Pro Leu Ile
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 Ala Gln Lys Tyr Tyr Leu Gly Ser Ser Ala His Lys Asn Leu Thr Glu
 130 135 140
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 His Pro Ser Pro Arg Asn Gln Ile Trp Leu Lys Lys Asn Pro Trp Phe
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 Lys Asp

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 Val Thr Pro Ser Asp Met Pro Asp Thr Lys Gln Leu Val Ser Asp Glu
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 Lys Val Ala Pro Ser Thr Leu Gln Asn Thr Pro Asp Lys Thr Ser Gln
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 Gly His Pro Val Glu Ser Thr Gly Leu Trp Ile Trp Gly Asp Val Asp
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 195 200 205
 Lys Lys Asp Asp Tyr Gly Tyr Val Asp Phe Lys Leu Ser Glu Lys
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 Gln Arg Lys Gln Ile Ser Phe Leu Ile Asn Asn Lys Ala Gly Thr Asn
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 Leu Ser Gly Asp His His Ile Pro Leu Leu Arg Pro Glu Met Asn Gln
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 Val Trp Ile Asp Glu Lys Tyr Gly Ile His Thr Tyr Gln Pro Leu Lys
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 Glu Gly Tyr Val Arg Ile Asn Tyr Leu Ser Ser Ser Asn Tyr Asp
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 His Leu Ser Ala Trp Leu Phe Lys Asp Val Ala Thr Xaa Ser Thr Thr
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 Trp Pro Asp Gly Ser Asn Phe Val Asn Gln Gly Leu Tyr Gly Arg Tyr
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 Ile Asp Val Ser Leu Lys Thr Asn Ala Lys Glu Ile Gly Phe Leu Ile
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 Leu Asp Glu Ser Lys Thr Gly Asp Ala Val Lys Val Gln Pro Asn Asp
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 Tyr Val Phe Arg Asp Leu Ala Asn His Asn Gln Ile Phe Val Lys Asp
 355 360 365
 Lys Asp Pro Lys Val Tyr Asn Asn Pro Tyr Tyr Ile Asp Gln Val Gln
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 Thr Thr Leu Asp Gly Val Asp Lys Thr Glu Ile Leu Lys Glu Leu Lys
 405 410 415
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 Ile Leu Asp Pro Tyr Ala Lys Ser Leu Ala Glu Trp Asp Ser Asn Thr
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 Gly Arg Gln Asp Ala Val Ile Tyr Glu Ala His Val Arg Asp Phe Thr
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 Ser Asp Arg Ser Leu Asp Gly Lys Leu Lys Asn Gln Phe Gly Thr Phe
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 Ala Ala Phe Ser Glu Lys Leu Asp Tyr Leu Gln Lys Leu Gly Val Thr
 645 650 655
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 675 680 685
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 690 695 700
 Glu Lys Pro Lys Asp Pro Ser Ala Arg Ile Ala Glu Leu Lys Gln Leu
 705 710 715 720
 Ile His Asp Ile His Lys Arg Gly Met Gly Val Ile Leu Asp Val Val
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 Tyr Asn His Thr Ala Lys Thr Tyr Leu Phe Glu Asp Ile Glu Pro Asn
 740 745 750
 Tyr Tyr His Phe Met Asn Glu Asp Gly Ser Pro Arg Glu Ser Phe Gly
 755 760 765
 Gly Gly Arg Leu Gly Thr Thr His Ala Met Ser Arg Arg Val Leu Val
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 Asp Ser Ile Lys Tyr Leu Thr Ser Glu Phe Lys Val Asp Gly Phe Arg
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 Lys Glu Ala Lys Ala Ile Asn Pro Asn Met Ile Met Ile Gly Glu Gly
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Lys Leu Gly Asp Glu Ile Asp Leu Glu Leu Leu Asp Thr Glu Lys Ser		
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Gly Lys Ile Lys Ser His Lys Phe Lys Ile Ile Gly Ile Phe Ser Gly		
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Glu Ser Thr Glu Leu Ala Leu Asn Lys Leu Lys Asp Phe Lys Ile Asp		
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agatgcaccc	tcgttacaat	caacaacaag	gtatccatca	ctatttacgt	gcgattttcag	2880
gtaagacagc	cgaactcttt	aaatttagta	gcaaaagaagg	agcttacttt	gttgggtcag	2940
agaaggaggt	tgttcgtcta	gcaggccata	tcggctttaa	cattgttatg	acattccaaa	3000
ttttggatga	tatcctggat	tatactgcag	ataaaaaaac	attnaataag	cctgtcttag	3060
aggatttaac	acaaggcggt	tacagccttc	ctctacttct	tgccattgaa	gaaaatcctg	3120
atatttcaaa	acctattttt	gataaaaaaa	cagatatggc	tactgaagac	atggaaaaaa	3180
ttgcttatct	cgtcgtttcc	catagagggt	ttgacaaagc	tcgccatcta	gctcgtaat	3240
ttacttgagaa	agcttattat	gacataaata	agctacccca	gaactctgca	aaaaaacagt	3300
tgctacaatt	aactaattac	cttttaaaac	gcaaaattta	aataataaaa	aaacattcca	3360
caatgctaga	aaagcagttt	ggaaatgttt	tttattttatc	attnaatttt	cgcacccatc	3420
aatcatcata	gatcaccatc	atcagccggct	ttcagctgac	gttaacgttg	actactttga	3480
gacaattctt	gaggagaacc	ttccaactct	aatttgcctt	tttctataaa	taagatacga	3540
tcagcatgtt	caataccctt	taagtatgt	gtaatccaaa	ctaaaggctt	accttccaaat	3600

tctttcataa atacccttag taaggcttgc tcagtaatag gatcaagtcc aacagttggc 3660
 tcatctaaga taacaattgg gacatctttt agtaagattc tagccaaagc aattctatgc 3720
 ctttcggcac ctgaaaacct aagtccagct tcatcaacca ttgtatagag accatctgat 3780
 aaatcagtga ccatctctt caatccaact cgttcaagaa ctttccatac atcttcttca 3840
 cttagcatctt ggtttccaat gcgaatgtta ttttagcaggg ttgtattaaa aaggttagggc 3900
 gcttgggtta tcactccaat atagttagaa atgcaatcac caactattga aacatcagca 3960
 cccgccttaggg taatcttccc ttgactgtct ttcagaatgcg cacgaagtag actagctaag 4020
 gtactcttgc cagaaccact ccgcctaaa atagcaattt tttctccttc tttaatatcc 4080
 aaatcttaat gatgcaaaaac ccatttctct tttggcttat actggaaaact taaattcttg 4140
 acggaaaaat catatggctt attaggcaat t 4171

<210> 33
 <211> 649
 <212> PRT
 <213> Streptococcus

<400> 33
 Tyr Asp Asn Ile Phe Gln Ser Leu His His Leu Leu Ala Cys Arg Gly
 1 5 10 15
 Lys Ser Gly Asn Thr Leu Ile Asp Gln Leu Val Ala Asp Gly Leu Leu
 20 25 30
 His Ala Asp Asn His Tyr His Phe Phe Asn Gly Lys Ser Leu Ala Thr
 35 40 45
 Phe Asn Thr Asn Gln Leu Ile Arg Glu Val Val Tyr Val Glu Ile Ser
 50 55 60
 Leu Asp Thr Met Ser Ser Gly Glu His Asp Leu Val Lys Val Asn Ile
 65 70 75 80
 Ile Arg Pro Thr Thr Glu His Thr Ile Pro Thr Met Met Thr Ala Ser
 85 90 95
 Pro Tyr His Gln Gly Ile Asn Asp Pro Ala Ala Asp Gln Lys Thr Tyr
 100 105 110
 Gln Met Glu Gly Ala Leu Ala Val Lys Gln Pro Lys His Ile Gln Val
 115 120 125
 Asp Thr Lys Pro Phe Lys Glu Val Lys His Pro Ser Lys Leu Pro
 130 135 140
 Ile Ser Pro Ala Thr Glu Ser Phe Thr His Ile Asp Ser Tyr Ser Leu
 145 150 155 160
 Asn Asp Tyr Phe Leu Ser Arg Gly Phe Ala Asn Ile Tyr Val Ser Gly
 165 170 175
 Val Gly Thr Ala Gly Ser Thr Gly Phe Met Thr Ser Gly Asp Tyr Gln
 180 185 190
 Gln Ile Gln Ser Phe Lys Ala Val Ile Asp Trp Leu Asn Gly Lys Val
 195 200 205
 Thr Ala Phe Thr Ser His Lys Arg Asp Lys Gln Val Lys Ala Asp Trp
 210 215 220
 Ser Asn Gly Leu Val Ala Thr Thr Gly Lys Ser Tyr Leu Gly Thr Met
 225 230 235 240
 Ser Thr Gly Leu Ala Thr Thr Gly Val Glu Gly Leu Lys Val Ile Ile
 245 250 255
 Ala Glu Ala Ala Ile Ser Thr Trp Tyr Asp Tyr Tyr Arg Glu Asn Gly
 260 265 270
 Leu Val Cys Ser Pro Gly Gly Tyr Pro Gly Glu Asp Leu Asp Val Leu
 275 280 285
 Thr Glu Leu Thr Tyr Ser Arg Asn Leu Leu Ala Gly Asp Tyr Ile Lys
 290 295 300
 Asn Asn Asp Cys Tyr Gln Ala Leu Leu Asn Glu Gln Ser Lys Ala Ile

305	310	315	320
Asp Arg Gln Ser Gly Asp Tyr Asn Gln Tyr Trp His Asp Arg Asn Tyr			
325	330	335	
Leu Thr His Val Asn Asn Val Lys Ser Arg Val Val Tyr Thr His Gly			
340	345	350	
Leu Gln Asp Trp Asn Val Lys Pro Arg His Val Tyr Lys Val Phe Asn			
355	360	365	
Ala Leu Pro Gln Thr Ile Lys His Leu Phe Leu His Gln Gly Gln			
370	375	380	
His Val Tyr Met His Asn Trp Gln Ser Ile Asp Phe Arg Glu Ser Met			
385	390	395	400
Asn Ala Leu Leu Ser Gln Glu Leu Leu Gly Ile Asp Asn His Phe Gln			
405	410	415	
Leu Glu Glu Val Ile Trp Gln Asp Asn Thr Thr Glu Gln Thr Trp Gln			
420	425	430	
Val Leu Asp Ala Phe Gly Gly Asn His Gln Glu Gln Ile Gly Leu Gly			
435	440	445	
Asp Ser Lys Lys Leu Ile Asp Asn His Tyr Asp Lys Glu Ala Phe Asp			
450	455	460	
Thr Tyr Cys Lys Asp Phe Asn Val Phe Lys Asn Asp Leu Phe Lys Gly			
465	470	475	480
Asn Asn Lys Thr Asn Gln Ile Thr Ile Asn Leu Pro Leu Lys Lys Asn			
485	490	495	
Tyr Leu Leu Asn Gly Gln Cys Lys Leu His Leu Arg Val Lys Thr Ser			
500	505	510	
Asp Lys Lys Ala Ile Leu Ser Ala Gln Ile Leu Asp Tyr Gly Pro Lys			
515	520	525	
Lys Arg Phe Lys Asp Thr Pro Thr Ile Lys Phe Leu Asn Ser Leu Asp			
530	535	540	
Asn Gly Lys Asn Phe Ala Arg Glu Ala Leu Arg Glu Leu Pro Phe Thr			
545	550	555	560
Lys Asp His Tyr Arg Val Ile Ser Lys Gly Val Leu Asn Leu Gln Asn			
565	570	575	
Arg Thr Asp Leu Leu Thr Ile Glu Ala Ile Glu Pro Glu Gln Trp Phe			
580	585	590	
Asp Ile Glu Phe Ser Leu Gln Pro Ser Ile Tyr Gln Leu Ser Lys Gly			
595	600	605	
Asp Asn Leu Arg Ile Ile Leu Tyr Thr Thr Asp Phe Glu His Thr Ile			
610	615	620	
Arg Asp Asn Ala Ser Tyr Ser Ile Thr Val Asp Leu Ser Gln Ser Tyr			
625	630	635	640
Leu Thr Ile Pro Thr Asn Gln Gly Asn			
645			

<210> 34
 <211> 119
 <212> PRT
 <213> Streptococcus

<400> 34
 Met Lys Leu Leu Thr Lys Glu Arg Phe Asp Asp Ser Gln His Phe Trp
 1 5 10 15
 Tyr Gln Ile Asn Leu Leu Gln Glu Ser Asn Phe Gly Ala Val Phe Asp
 20 25 30
 His Asp Asn Lys Asn Ile Pro Gln Val Val Ala Thr Ile Val Asp Asp
 35 40 45

Leu Gln Gly Ser Gly Ser Ser Asn His Phe Trp Tyr Phe Gly Asn Thr
 50 55 60
 Thr Asp Thr Ser Ile Leu Met Ile Ala His Leu Asn Arg Lys Phe Tyr
 65 70 75 80
 Ile Gln Val Asn Leu Lys Asp Phe Asp Phe Ala Leu Asn Leu Ile Ala
 85 90 95
 Ile Asn Asn Trp Lys Ser Leu Leu Gln Thr Gln Leu Glu Ala Leu Asn
 100 105 110
 Asp Thr Leu Ala Ile Phe Gln
 115

<210> 35
 <211> 326
 <212> PRT
 <213> Streptococcus

<400> 35
 Met Ser Ser Tyr Trp Asn Asn Tyr Pro Glu Leu Lys Lys Asn Ile Asp
 1 5 10 15
 Glu Thr Asn Gln Leu Ile Gln Glu Arg Ile Gln Val Arg Asn Lys Asp
 20 25 30
 Ile Glu Ala Ala Leu Ser Gln Leu Thr Ala Ala Gly Gly Lys Gln Leu
 35 40 45
 Arg Pro Ala Phe Phe Tyr Leu Phe Ser Gln Leu Gly Asn Lys Glu Asn
 50 55 60
 Gln Asp Thr Gln Gln Leu Lys Lys Ile Ala Ala Ser Leu Glu Ile Leu
 65 70 75 80
 His Val Ala Thr Leu Ile His Asp Asp Val Ile Asp Asp Ser Pro Leu
 85 90 95
 Arg Arg Gly Asn Met Thr Ile Gln Ser Lys Phe Gly Lys Asp Ile Ala
 100 105 110
 Val Tyr Thr Gly Asp Leu Leu Phe Thr Val Phe Phe Asp Leu Ile Leu
 115 120 125
 Glu Ser Met Thr Asp Thr Pro Phe Met Arg Ile Asn Ala Lys Ser Met
 130 135 140
 Arg Lys Ile Leu Met Gly Glu Leu Asp Gln Met His Leu Arg Tyr Asn
 145 150 155 160
 Gln Gln Gln Gly Ile His His Tyr Leu Arg Ala Ile Ser Gly Lys Thr
 165 170 175
 Ala Glu Leu Phe Lys Leu Ala Ser Lys Glu Gly Ala Tyr Phe Gly Gly
 180 185 190
 Ala Glu Lys Glu Val Val Arg Leu Ala Gly His Ile Gly Phe Asn Ile
 195 200 205
 Gly Met Thr Phe Gln Ile Leu Asp Asp Ile Leu Asp Tyr Thr Ala Asp
 210 215 220
 Lys Lys Thr Phe Asn Lys Pro Val Leu Glu Asp Leu Thr Gln Gly Val
 225 230 235 240
 Tyr Ser Leu Pro Leu Leu Leu Ala Ile Glu Glu Asn Pro Asp Ile Phe
 245 250 255
 Lys Pro Ile Leu Asp Lys Lys Thr Asp Met Ala Thr Glu Asp Met Glu
 260 265 270
 Lys Ile Ala Tyr Leu Val Val Ser His Arg Gly Val Asp Lys Ala Arg
 275 280 285
 His Leu Ala Arg Lys Phe Thr Glu Lys Ala Ile Ser Asp Ile Asn Lys
 290 295 300
 Leu Pro Gln Asn Ser Ala Lys Lys Gln Leu Leu Gln Leu Thr Asn Tyr

305	310	315	320
Leu	Leu	Lys	Arg
		Lys	Ile
			325

<210> 36
 <211> 247
 <212> PRT
 <213> Streptococcus

<400> 36
 Leu Pro Asn Lys Pro Tyr Asp Phe Ser Val Lys Asn Leu Ser Phe Gln
 1 5 10 15
 Tyr Lys Pro Gln Glu Lys Trp Val Leu His His Leu Asp Leu Asp Ile
 20 25 30
 Lys Glu Gly Glu Lys Ile Ala Ile Leu Gly Arg Ser Gly Ser Gly Lys
 35 40 45
 Ser Thr Leu Ala Ser Leu Leu Arg Gly Asp Leu Lys Ala Ser Gln Gly
 50 55 60
 Lys Ile Thr Leu Gly Gly Ala Asp Val Ser Ile Val Gly Asp Cys Ile
 65 70 75 80
 Ser Asn Tyr Ile Gly Val Ile Gln Gln Ala Pro Tyr Leu Phe Asn Thr
 85 90 95
 Thr Leu Leu Asn Asn Ile Arg Ile Gly Asn Gln Asp Ala Ser Glu Glu
 100 105 110
 Asp Val Trp Lys Val Leu Glu Arg Val Gly Leu Lys Glu Met Val Thr
 115 120 125
 Asp Leu Ser Asp Gly Leu Tyr Thr Met Val Asp Glu Ala Gly Leu Arg
 130 135 140
 Phe Ser Gly Gly Glu Arg His Arg Ile Ala Leu Ala Arg Ile Leu Leu
 145 150 155 160
 Lys Asp Val Pro Ile Val Ile Leu Asp Glu Pro Thr Val Gly Leu Asp
 165 170 175
 Pro Ile Thr Glu Gln Ala Leu Leu Arg Val Phe Met Lys Glu Leu Glu
 180 185 190
 Gly Lys Thr Leu Val Trp Ile Thr His His Leu Lys Gly Ile Glu His
 195 200 205
 Ala Asp Arg Ile Leu Phe Ile Glu Asn Gly Gln Leu Glu Leu Glu Gly
 210 215 220
 Ser Pro Gln Glu Leu Ser Gln Ser Ser Gln Arg Tyr Arg Gln Leu Lys
 225 230 235 240
 Ala Ala Asp Asp Gly Asp Leu
 245

<210> 37
 <211> 3480
 <212> DNA
 <213> Streptococcus

<400> 37
 aattctatTTT ggaggTTTTT cttgaataaa tggtagtta aggcaagtTC cttagTTgtt 60
 ttaggtgta tggTTTATC tgcgggTTCC cgagTTtag cggtactta tgtccgtCCA 120
 attgataatg gtagaattac aacaggtTC aatggTTATC ctggacattg tggggTggat 180
 tatgctgTTc cgactggAAC gattattagg gcagtggcag atggTactgt gaaatttgca 240
 ggagctggag ccaactTTc ttggatgaca gacttagcag gaaattgtgt catgattcaa 300
 catgcggatg gaatgcatag tggTACGCT catatgtcac gtgtggTggc taggactggg 360
 gaaaaagtca aacaaggaga tatcatcggt tacgttaggag caactggTat ggcgacggg 420

cctcaccc	tttgcattt	tttaccagct	aaccctaatt	ttcaaaatgg	tttccatgga	480
cgtatca	tc	caacgtca	aattgcta	ac	gttgcgac	540
tc	tc	gcattaa	gcca	attaca	atca	600
aa	aa	gat	gat	aa	tttggaa	660
acc	cc	cgact	gggtt	tgat	gat	720
gagg	tt	ctaa	atgg	tttgcac	gaccagg	780
atctt	ta	ctaa	actct	taa	gactgt	840
acttgg	gg	ca	acacgc	tttgc	tttgc	900
caaga	ttt	aca	actgc	tttgc	tttgc	960
tacta	actaa	gt	acaattt	ttt	aaaaccgt	1020
tgat	atttata	gt	tcg	tttgc	tttgc	1080
aaaagg	tact	tttgc	tttgc	tttgc	tttgc	1140
caca	aa	aa	ac	tttgc	tttgc	1200
taa	aa	aa	aa	tttgc	tttgc	1260
caga	aa	aa	aa	tttgc	tttgc	1320
atctt	attt	tc	c	tttgc	tttgc	1380
cttca	atgaa	aa	at	tttgc	tttgc	1440
attt	gaaa	aa	at	tttgc	tttgc	1500
aagg	tat	ca	at	tttgc	tttgc	1560
cgcc	cag	cc	at	tttgc	tttgc	1620
cta	atgac	cc	at	tttgc	tttgc	1680
aag	agg	cc	at	tttgc	tttgc	1740
ctgtt	gc	tttgc	tttgc	tttgc	tttgc	1800
ccc	ctt	tttgc	tttgc	tttgc	tttgc	1860
agc	atgt	tttgc	tttgc	tttgc	tttgc	1920
taca	agg	tttgc	tttgc	tttgc	tttgc	1980
tag	caca	tttgc	tttgc	tttgc	tttgc	2040
aa	cata	tttgc	tttgc	tttgc	tttgc	2100
gtac	atcc	tttgc	tttgc	tttgc	tttgc	2160
tag	aaaa	tttgc	tttgc	tttgc	tttgc	2220
caa	ata	tttgc	tttgc	tttgc	tttgc	2280
atgg	acc	tttgc	tttgc	tttgc	tttgc	2340
atg	acc	tttgc	tttgc	tttgc	tttgc	2400
ttt	ttt	tttgc	tttgc	tttgc	tttgc	2460
tta	agc	tttgc	tttgc	tttgc	tttgc	2520
taaa	atc	tttgc	tttgc	tttgc	tttgc	2580
tag	atc	tttgc	tttgc	tttgc	tttgc	2640
cttt	aaaa	tttgc	tttgc	tttgc	tttgc	2700
ctct	tttata	tttgc	tttgc	tttgc	tttgc	2760
gag	cgtt	tttgc	tttgc	tttgc	tttgc	2820
tttt	atcc	tttgc	tttgc	tttgc	tttgc	2880
ctac	gtat	tttgc	tttgc	tttgc	tttgc	2940
gtac	actt	tttgc	tttgc	tttgc	tttgc	3000
ggaa	at	tttgc	tttgc	tttgc	tttgc	3060
cttt	gaag	tttgc	tttgc	tttgc	tttgc	3120
gcca	aga	tttgc	tttgc	tttgc	tttgc	3180
tgat	ttc	tttgc	tttgc	tttgc	tttgc	3240
ttgc	cagg	tttgc	tttgc	tttgc	tttgc	3300
tctc	aggact	tttgc	tttgc	tttgc	tttgc	3360
gtt	atgat	tttgc	tttgc	tttgc	tttgc	3420
tttgc	tttgc	tttgc	tttgc	tttgc	tttgc	3480

<210> 38
 <211> 306
 <212> PRT
 <213> Streptococcus

<400> 38
 Asn Ser Ile Trp Arg Phe Phe Leu Asn Lys Trp Leu Val Lys Ala Ser
 1 5 10 15
 Ser Leu Val Val Leu Gly Gly Met Val Leu Ser Ala Gly Ser Arg Val
 20 25 30
 Leu Ala Asp Thr Tyr Val Arg Pro Ile Asp Asn Gly Arg Ile Thr Thr
 35 40 45
 Gly Phe Asn Gly Tyr Pro Gly His Cys Gly Val Asp Tyr Ala Val Pro
 50 55 60
 Thr Gly Thr Ile Ile Arg Ala Val Ala Asp Gly Thr Val Lys Phe Ala
 65 70 75 80
 Gly Ala Gly Ala Asn Phe Ser Trp Met Thr Asp Leu Ala Gly Asn Cys
 85 90 95
 Val Met Ile Gln His Ala Asp Gly Met His Ser Gly Tyr Ala His Met
 100 105 110
 Ser Arg Val Val Ala Arg Thr Gly Glu Lys Val Lys Gln Gly Asp Ile
 115 120 125
 Ile Gly Tyr Val Gly Ala Thr Gly Met Ala Thr Gly Pro His Leu His
 130 135 140
 Phe Glu Phe Leu Pro Ala Asn Pro Asn Phe Gln Asn Gly Phe His Gly
 145 150 155 160
 Arg Ile Asn Pro Thr Ser Leu Ile Ala Asn Val Ala Thr Phe Ser Gly
 165 170 175
 Lys Thr Gln Ala Ser Ala Pro Ser Ile Lys Pro Leu Gln Ser Ala Pro
 180 185 190
 Val Gln Asn Gln Ser Ser Lys Leu Lys Val Tyr Arg Val Asp Glu Leu
 195 200 205
 Gln Lys Val Asn Gly Val Trp Leu Val Lys Asn Asn Thr Leu Thr Pro
 210 215 220
 Thr Gly Phe Asp Trp Asn Asp Asn Gly Ile Pro Ala Ser Glu Ile Asp
 225 230 235 240
 Glu Val Asp Ala Asn Gly Asn Leu Thr Ala Asp Gln Val Leu Gln Lys
 245 250 255
 Gly Gly Tyr Phe Ile Phe Asn Pro Lys Thr Leu Lys Thr Val Glu Lys
 260 265 270
 Pro Ile Gln Gly Thr Ala Gly Leu Thr Trp Ala Lys Thr Arg Phe Ala
 275 280 285
 Asn Gly Ser Ser Val Trp Leu Arg Val Asp Asn Ser Gln Glu Leu Leu
 290 295 300
 Tyr Lys
 305

<210> 39
 <211> 434
 <212> PRT
 <213> Streptococcus

<400> 39
 Met Lys Met Asn Lys Lys Val Leu Leu Thr Ser Thr Met Ala Ala Ser
 1 5 10 15
 Leu Leu Ser Val Ala Ser Val Gln Ala Gln Glu Thr Asp Thr Thr Trp
 20 25 30
 Thr Ala Arg Thr Val Ser Glu Val Lys Ala Asp Leu Val Lys Gln Asp
 35 40 45
 Asn Lys Ser Ser Tyr Thr Val Lys Tyr Gly Asp Thr Leu Ser Val Ile

50	55	60													
Ser	Glu	Ala	Met	Ser	Ile	Asp	Met	Asn	Val	Leu	Ala	Lys	Ile	Asn	Asn
65															80
Ile	Ala	Asp	Ile	Asn	Leu	Ile	Tyr	Pro	Glu	Thr	Thr	Leu	Thr	Val	Thr
															95
Tyr	Asp	Gln	Lys	Ser	His	Thr	Ala	Thr	Ser	Met	Lys	Ile	Glu	Thr	Pro
															110
100															
Ala	Thr	Asn	Ala	Ala	Gly	Gln	Thr	Thr	Ala	Thr	Val	Asp	Leu	Lys	Thr
															125
115															
Asn	Gln	Val	Ser	Val	Ala	Asp	Gln	Lys	Val	Ser	Leu	Asn	Thr	Ile	Ser
															140
130															
Glu	Gly	Met	Thr	Pro	Glu	Ala	Ala	Thr	Thr	Ile	Val	Ser	Pro	Met	Lys
															160
145															
Thr	Tyr	Ser	Ser	Ala	Pro	Ala	Leu	Lys	Ser	Lys	Glu	Val	Leu	Ala	Gln
															175
165															
Glu	Gln	Ala	Val	Ser	Gln	Ala	Ala	Asn	Glu	Gln	Val	Ser	Thr	Ala	
															190
180															
Pro	Val	Lys	Ser	Ile	Thr	Ser	Glu	Val	Pro	Ala	Ala	Lys	Glu	Glu	Val
															205
195															
Lys	Pro	Thr	Gln	Thr	Ser	Val	Ser	Gln	Ser	Thr	Thr	Val	Ser	Pro	Ala
															220
210															
Ser	Val	Ala	Ala	Glu	Thr	Pro	Ala	Pro	Val	Ala	Lys	Val	Ala	Pro	Val
															240
225															
Arg	Thr	Val	Ala	Ala	Pro	Arg	Val	Ala	Ser	Val	Lys	Val	Val	Thr	Pro
															255
245															
Lys	Val	Glu	Thr	Gly	Ala	Ser	Pro	Glu	His	Val	Ser	Ala	Pro	Ala	Val
															270
260															
Pro	Val	Thr	Thr	Ser	Thr	Ala	Thr	Asp	Ser	Lys	Leu	Gln	Ala	Thr	
															285
275															
Glu	Val	Lys	Ser	Val	Pro	Val	Ala	Gln	Lys	Ala	Pro	Thr	Ala	Thr	Pro
															300
290															
Val	Ala	Gln	Pro	Ala	Ser	Thr	Thr	Asn	Ala	Val	Ala	Ala	His	Pro	Glu
															320
305															
Asn	Ala	Gly	Leu	Gln	Pro	His	Val	Ala	Ala	Tyr	Lys	Glu	Lys	Val	Ala
															335
325															
Ser	Thr	Tyr	Gly	Val	Asn	Glu	Phe	Ser	Thr	Tyr	Arg	Ala	Gly	Asp	Pro
															350
340															
Gly	Asp	His	Gly	Lys	Gly	Leu	Ala	Val	Asp	Phe	Ile	Val	Gly	Lys	Asn
															365
355															
Gln	Ala	Leu	Gly	Asn	Glu	Val	Ala	Gln	Tyr	Ser	Thr	Gln	Asn	Met	Ala
															380
370															
Ala	Asn	Asn	Ile	Ser	Tyr	Val	Ile	Trp	Gln	Gln	Lys	Phe	Tyr	Ser	Asn
															400
385															
Thr	Asn	Ser	Ile	Tyr	Gly	Pro	Ala	Asn	Thr	Trp	Asn	Ala	Met	Pro	Asp
															415
405															
Arg	Gly	Gly	Val	Thr	Ala	Asn	His	Tyr	Asp	His	Val	His	Val	Ser	Phe
															430
420															
Asn	Lys														

<210> 40
 <211> 232
 <212> PRT
 <213> Streptococcus
 <400> 40

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 Ile Ile Val Ser Cys Gln Ala Leu Pro Gly Glu Pro Leu Tyr Thr Glu
 20 25 30
 Ser Gly Gly Val Met Pro Leu Leu Ala Ala Gln Glu Ala Gly
 35 40 45
 Ala Val Gly Ile Arg Ala Asn Ser Val Arg Asp Ile Lys Glu Ile Gln
 50 55 60
 Glu Val Thr Asn Leu Pro Ile Ile Gly Ile Ile Lys Arg Glu Tyr Pro
 65 70 75 80
 Pro Gln Glu Pro Phe Ile Thr Ala Thr Met Thr Glu Val Asp Gln Leu
 85 90 95
 Ala Ser Leu Asp Ile Ala Val Ile Ala Leu Asp Cys Thr Leu Arg Glu
 100 105 110
 Arg His Asp Gly Leu Ser Val Ala Glu Phe Ile Gln Lys Ile Lys Gly
 115 120 125
 Lys Tyr Pro Glu Gln Leu Leu Met Ala Asp Ile Ser Thr Phe Glu Glu
 130 135 140
 Gly Lys Asn Ala Phe Glu Ala Gly Val Asp Phe Val Gly Thr Thr Leu
 145 150 155 160
 Ser Gly Tyr Thr Asp Tyr Xaa Arg Gln Glu Glu Gly Pro Asp Ile Glu
 165 170 175
 Leu Leu Asn Lys Leu Cys Gln Ala Gly Ile Asp Val Ile Ala Glu Gly
 180 185 190
 Lys Ile His Thr Pro Lys Gln Ala Asn Glu Ile Asn His Ile Gly Val
 195 200 205
 Ala Gly Ile Val Val Gly Ala Ile Thr Arg Pro Lys Glu Ile Ala
 210 215 220
 Glu Arg Phe Ile Ser Gly Leu Ser
 225 230

<210> 41
 <211> 39
 <212> PRT
 <213> Streptococcus

<400> 41
 Met Ser Ile Lys Lys Ser Val Ile Gly Phe Cys Leu Gly Ala Ala Ala
 1 5 10 15
 Leu Ser Met Phe Ala Cys Val Asp Ser Ser Gln Ser Val Met Ala Ala
 20 25 30
 Glu Lys Asp Lys Val Glu Ile
 35

<210> 42
 <211> 1305
 <212> DNA
 <213> Streptococcus

<400> 42
 atgaaaatga ataaaaaggt actattgaca tcgacaatgg cagcttcgct attatcagtc 60
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 aaggctgatt tggtaaagca agacaataaa tcatcatata ctgtgaaata tggtgataca 180
 ctaagcgat tttcagaagc aatgtcaatt gatatgaatg tcttagaaa aattaataac 240
 attgcagata tcaatcttat ttatccgttgc acaacactga cagtaactta cgatcagaag 300
 agtcatactg ccacttcaat gaaaatagaa acaccagcaa caaatgctgc tggtcaaaca 360

acagctactg tggatttgaa aaccatcaa gtttctgttg cagacaaaa agtttctctc 420
 aatacaattt cggaaggtat gacaccagaa gcagcaacaa cgattttc gccaatgaag 480
 acatattttt ctgcgccagc tttgaatca aaagaagtt tagcacaaga gcaagctgtt 540
 agtcaagcag cagctaatttca acaggtatca acagctcctg tgaagtcgt tacttcagaa 600
 gttccagcag ctaaaagagga agttaaaacca actcagacgt cagtcagtca gtcaacaaca 660
 gtatcaccag cttctgttgc cgctgaaaca ccagctccag tagctaaatg agcaccggta 720
 agaactgttag cagccctag agtggcaagt gttaaaggtag tcactcttaa agtagaaact 780
 ggtgcacatcac cagagcatgt atcagctcca gcagttcctg tgactacgac ttcaacagct 840
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Ala Tyr Lys Glu Lys Val Ala Ser Thr Tyr Gly Val Asn Glu Phe Ser		
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Thr Tyr Arg Ala Gly Asp Pro Gly Asp His Gly Lys Gly Leu Ala Val		
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Asp His Val His Val Ser Phe Asn Lys		
405		



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number:	PCT/CA99/00114		(74) Agents: CÔTE, France et al.; Swabey Ogilvy Renault, Suite 1600, 1981 McGill College Avenue, Montréal, Québec H3A 2Y3 (CA).
(22) International Filing Date:	17 February 1999 (17.02.99)		
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(71) Applicant (for all designated States except US): BIOCHEM VACCINS INC. [CA/CA]; 2323 boulevard du Parc Technologique, Sainte-Foy, Québec G1P 4R8 (CA).			
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<p>Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(88) Date of publication of the international search report: 23 March 2000 (23.03.00)</p>			

(54) Title: GROUP B STREPTOCOCCUS ANTIGENS

(57) Abstract

Group B streptococcus (GBS) proteins and polynucleotides encoding them are disclosed. Said proteins are antigenic and therefore useful vaccine components for the prophylaxis or therapy of streptococcus infection in animals. Also disclosed are recombinant methods of producing the protein antigens as well as diagnostic assays for detecting streptococcus bacterial infection.

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INTERNATIONAL SEARCH REPORT

Interr. Application No
PCT/CA 99/00114A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/31 C07K14/315 A61K39/09 C12N1/21

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MICHEL J L ET AL: "Cloned alpha and beta C-protein antigens of group B Streptococci elicit protective immunity" INFECTION AND IMMUNITY, vol. 59, no. 6, June 1991 (1991-06), pages 2023-2028, XP002107260 AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON., US ISSN: 0019-9567 the whole document</p> <p>---</p> <p style="text-align: center;">-/-</p>	1-48

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

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Date of the actual completion of the international search

15 December 1999

Date of mailing of the international search report

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Authorized officer

Lejeune, R

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 99/00114

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LACHENAUER C S ET AL: "Cloning and expression in <i>Escherichia coli</i> of a protective surface protein from type V group B <i>Streptococci</i>" <i>ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY</i>, vol. 418, 9 December 1997 (1997-12-09), pages 615-618, XP002107261 SPRING ST., NY, US ISSN: 0065-2598 the whole document ---</p>	1-48
P,X	<p>DATABASE EMBL [Online] Accession number AF062533, 11 February 1999 (1999-02-11) SPELLERBERG B ET AL: "Streptococcus agalactiae Lmb (lmb) gene, complete cds; and unknown gene." XP002125180 98.9% identity between base 1-2514 of SEQ ID NO 13 and base 988-3501 of AF062533 Translation product (AC: Q9ZH9) has 98.5% identity in 793 AA overlap with SEQ ID NO 15 and 98.5% identity in 715 AA overlap with SEQ ID 16 & SPELLERBERG B ET AL: "Lmb, a protein with similarities to the LraI adhesin family, mediates attachment of <i>Streptococcus agalactiae</i> to human laminin" <i>INFECTION AND IMMUNITY</i>, vol. 67, no. 2, February 1999 (1999-02), pages 871-878, AMERICAN SOCIETY FOR MICROBIOLOGY. WASHINGTON., US ISSN: 0019-9567 ---</p>	1-10, 16-23,26
X	<p>DATABASE EMBL [Online] Accession Number L23843, 4 January 1994 (1994-01-04) MACRINA F L ET AL: "ISN IS199 from <i>Streptococcus mutans</i> IS3 (Brathall serotype C) DNA fragment" XP002125181 79.6% identity between base 5212-4314 of SEQ ID NO 13 and base 312-1220 of L23843 Translation has 83.4% identity in 283 AA overlap with SEQ ID NO 21 ----</p>	1,3-7,10

INTERNATIONAL SEARCH REPORT

International Application No
PCT/CA 99/00114

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE EMBL [Online] Accession Number AF026542, 15 October 1997 (1997-10-15) HYNES W L ET AL: "Streptococcus pyogenes FF22 lantibiotic (scn) gene cluster region containing: scnK, scnR, streptococcin A-FF22 precursor (scnA), scnA1, scnM, scnT, scnF, scnE, scnG genes, complete cds, and tnpA gene, partial cds." XP002125182 88.2% identity between base 2607-2953 of SEQ ID NO 13 and base 10435-10777 of AF026542 Translation product (AC: 031057) has 95.8% identity in 71 AA overlap with SEQ ID NO 17 ---</p>	1-10, 16-23, 26
P,X	<p>DATABASE GENESEQ [Online] Accession Number V52136, 23 October 1998 (1998-10-23) BARASH S C ET AL: "Streptococcus pneumoniae genome fragment SEQ ID NO:3" XP002125183 68.5% identity between base 2539-3319 of SEQ ID NO 37 and base 18492-19271 of V52136 Translation has 74.5% identity in 231 AA overlap with SEQ ID NO 40 & WO 98 18931 A (DOUGHERTY BRIAN A ; HUMAN GENOME SCIENCES INC (US); ROSEN CRAIG A) 7 May 1998 (1998-05-07) -----</p>	1,3-7,10

INTERNATIONAL SEARCH REPORT

Int. ational application No.
PCT/CA 99/00114

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 37-46 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

As a result of the prior review under R. 40.2(e) PCT,
no additional fees are to be refunded.

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
11-14, 16, 24, 25, 27, 28, 30, 31 (completely), 1-10, 15, 17-23, 26, 29, 32-48 (all partially) i.e. (group of) inventions 1, 3 and 7
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

An isolated polynucleotide encoding a polypeptide having a sequence selected from the group consisting of SEQ ID 2, SEQ ID NO 3, SEQ ID NO 4, SEQ ID NO 5, SEQ ID NO 6 i.e. the open reading frames of clone 1 (SEQ ID NO 1). Also a vector comprising the polynucleotide, a host cell transformed therewith, an isolated polypeptide encoded by the polynucleotide, a vaccine composition comprising said polypeptide and a polynucleotide having a sequence SEQ ID NO 1.

2. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 2 (SEQ ID 7) with sequences SEQ ID NO 8-12.

3. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 3 (SEQ ID 13) with sequences SEQ ID NO 14-21.

4. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 4 (SEQ ID 22) with sequences SEQ ID NO 23-26.

5. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 5 (SEQ ID 27) with sequences SEQ ID NO 28-31.

6. Claims: 1-10,15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 6 (SEQ ID 32) with sequences SEQ ID NO 33-36.

7. Claims: 11-14,16,24,25,27,28,30,31 (all completely), 1-10, 15,17-23,26,29,32-48 (all partially)

Same as invention 1, but directed at polypeptides of clone 7 (SEQ ID 37) with sequences SEQ ID NO 38-41.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 99/00114

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9818931	A 07-05-1998	AU	5194598 A	22-05-1998
		AU	6909098 A	22-05-1998
		EP	0942983 A	22-09-1999
		EP	0941335 A	15-09-1999
		WO	9818930 A	07-05-1998